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*Journal of the Minnesota State Medical Association, Southern Minnesota Medical Association, Northern Minnesota Medical Association, Minnesota Academy of Medicine and Minneapolis Surgical Society*

**Volume 35** **July, 1952** **Number 7**

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Minnesota Medicine

*Journal of the Minnesota State Medical Association, Southern Minnesota Medical Association, Northern Minnesota Medical Association, Minnesota Academy of Medicine and Minneapolis Surgical Society*

Volume 35 July, 1952 Number 7

# ABUSES OF CORTISONE AND CORTICOTROPIN

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CORTISONE and corticotropin (ACTH) are active biologic substances which directly or indirectly affect many tissues and physiologic processes of the body.[13,26,27] Adequate clinical and experimental evidence demonstrates that either an excess or a deficiency of these hormones results in various pathologic changes. Convincing evidence also exists that the quantity of these hormones which is necessary to maintain homeostasis and a state of health may vary under different circumstances, and that the quantity of cortisone or similar hormones produced by the cortex of the adrenal gland can be altered by a variety of stimuli.

While the effects of corticotropin and cortisone that have been described to date justify such general statements as those above, little is known concerning the precise mode of action of these hormones. Likewise, though many physicians have acquired extensive experience with the use of cortisone and corticotropin during the past three years, the limits of therapeutic usefulness and the hazards of these hormones are not yet precisely defined. Consequently, any discussion of the abuses and hazards of the use of corticotropin and cortisone at this time represents only a current appraisal of a rapidly developing subject.

## Contraindications

In view of the extremely broad physiologic and clinical effects of cortisone and corticotropin, it is not surprising that patients with some diseases would be adversely affected, and that the presence of these diseases would constitute at least a relative contraindication to the use of the hormones. A number of these contraindications exist but only peptic ulcer, tuberculosis and emotional disturbances will be considered.

*Gastrointestinal Ulceration.*—In 1945, Ingle and his associates[16] observed deep ulcers in the prepyloric portion of the stomachs of two rats that had received large doses of compound F. One rat also had several ulcers in the cecum. Gastrointestinal ulceration in rats subjected to various forms of stress has been described by Selye,[23] and it has been postulated that excess secretion of adrenal cortical hormones was a factor in the development of ulceration.

Gray and associates[8] observed that, when corticotropin in doses ranging from 100 to 160 mg. was administered intramuscularly daily to normal persons for periods of three to four weeks, there was an increase of approximately 200 per cent in basal and nocturnal gastric secretion of acid and pepsin. Oral and parenteral administration of 250 mg. of cortisone daily to normal persons resulted in a similar gastric response. The maximal effects on gastric secretion of acid and pepsin were observed after seven to fourteen days of administration of the hormones.

Since the advent of therapy with corticotropin and cortisone, a number of reports[1,8,9,18,24] have appeared which describe massive gastric hemorrhage and the onset, reactivation or perforation of peptic ulcers during treatment with these hormones. In some of these cases, there was evidence of previous peptic ulcer, while in others there was nothing in the history to suggest that

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the patient had peptic ulcer prior to treatment with corticotropin or cortisone.

While coincidence cannot as yet be excluded completely, the reports just mentioned constitute strong circumstantial evidence that gastrointestinal ulceration and hemorrhage may be complications of therapy with corticotropin and cortisone and that administration of these hormones may be hazardous for the patient with peptic ulcer.

*Tuberculosis.*—A number of investigations[10,20,-25] have been reported in which administration of cortisone to animals before and after such animals were inoculated with Mycobacterium tuberculosis resulted in the occurrence of more extensive lesions or a higher mortality than was noted in a similarly inoculated group of control animals that did not receive cortisone. Freeman and associates[6] observed that while the systemic symptoms in patients with disseminated infiltrative pulmonary tuberculosis were ameliorated by administration of corticotropin, the sputum continued to show acid-fast bacilli. In one patient there was a definite spread of the pulmonary lesion during such therapy. Symptomatic improvement and a general feeling of well-being occurred in thirteen patients with advanced pulmonary tuberculosis who were treated with corticotropin and para-aminosalicylic acid.[29] However, roentgenologic examination in these cases indicated a greater tendency to cavitation. Rapidly progressive fatal pulmonary tuberculosis has been reported in one patient who received cortisone and in one patient who received corticotropin for rheumatoid arthritis.[5,17] During treatment with cortisone for arthritis, another patient with apparently arrested pulmonary tuberculosis experienced formation of a cavity and appearance of Mycobacterium tuberculosis in the sputum.[21]

Present evidence suggests that, in some unknown manner, cortisone is capable of suppressing the reaction of inflammation that occurs in response to a wide variety of different agents. If such reaction of inflammation is undesirable and detrimental, then cortisone and corticotropin, by virtue of this suppressive effect, would favorably modify the disease in question. However, if the changes produced by inflammation are desirable or protective, then cortisone and corticotropin might adversely affect the patient. While there is not sufficient evidence at present to justify a definite conclusion, the use of these hormones in most patients with tuberculosis is best avoided.

*Emotional Disturbances.*—Numerous reports [2,11,19,22,27] have called attention to the elevation of mood and euphoria which frequently accompany therapy with corticotropin or cortisone. This elevation of mood or euphoria seems to be the most frequent psychologic response to therapy with cortisone and corticotropin, and its presence usually does not present a serious problem. However, other more profound and serious psychologic disturbances have been observed occasionally during therapy with these hormones.[22] Psychoneurotic or frankly psychotic reactions may occur. Rome and Braceland[22] were of the opinion that the incidence of psychosis and psychoneurosis in patients who received corticotropin and cortisone probably exceeds the incidence of these reactions that would be expected in a group of patients who did not receive these hormones.

Rome and Braceland[22] also pointed out that the pattern of the psychologic response to therapy with corticotropin and cortisone is dependent on many elements. In their opinion, one of the most important factors that determine the clinical form of this response is the previous organization of the patient's personality. They observed that the psychotic reactions apparently occurred in patients who displayed evidence of marginal psychologic adjustment in the past. In view of these reports, it appears wise to avoid administration of cortisone and corticotropin in chronic diseases such as rheumatoid arthritis when these diseases occur in patients who are emotionally ill or who give a history of former serious emotional illness.

Since the presence of some diseases constitutes a relative contraindication to the use of cortisone and corticotropin, a careful and thorough general examination should always precede prolonged therapy with these hormones. The history should include careful evaluation of present and past gastrointestinal complaints and disturbances. Likewise, the physician should evaluate the patient's present emotional status and include in the history a survey of any past emotional illnesses as well as the patient's past general psychologic adjustment. The general examination should also include either roentgenographic or roentgenoscopic examination of the thorax unless the patient has recently had such an examination. Probably one of the more frequent abuses of cortisone and corticotropin in the therapy of chronic disease is the omission of a careful general examination before a prolonged course of therapy is begun.

## Dosage

Present evidence indicates that what might be an ideal dose of cortisone or corticotropin in some situations would not be the ideal dose in other situations. The various doses indicated for the use of cortisone in chronic adrenal insufficiency, in diseases without adrenal insufficiency and during periods of induced adrenal suppression will be discussed.

*Chronic Adrenal Insufficiency.*—Patients with chronic adrenal insufficiency that is due to primary disease of the adrenal gland or that is secondary to insufficiency of the anterior part of the pituitary gland show an excellent clinical response to small doses of cortisone. Usually, the daily maintenance dose is 25 mg. or less of cortisone, given orally in divided doses. Some patients do well on as little as 10 mg. of cortisone per day and others require 20 to 25 mg. per day. Not only do these patients feel well on small doses of cortisone, but they appear to be quite sensitive to the hormone and do not tolerate large daily doses. While the activity of orally administered cortisone is rapid in onset, the duration of its activity is relatively short. This fact is not generally appreciated. Two common errors in the use of cortisone by mouth in the therapy of chronic adrenal cortical insufficiency are the administration of an excessive dose and the utilization of a single dose rather than divided doses.

While administration of 25 mg. or less of cortisone provides good clinical response under ordinary circumstances in patients with chronic adrenal insufficiency, this is an inadequate dose under conditions of stress such as are encountered in serious injury, surgical procedures, acute illness and the crises of adrenal insufficiency. Under these circumstances, doses of 100 to 200 mg. daily are usually required.

*Diseases Without Adrenal Insufficiency.*—In contrast to the small group of patients just mentioned who receive cortisone as a form of replacement therapy, most patients receive cortisone and corticotropin in an attempt to modify favorably diseases in which there is at present no good evidence of adrenal cortical dysfunction or insufficiency. If the disease is acute and self-limited and treatment is necessary for only a short period, the clinical symptoms can usually be suppressed successfully by the use of relatively large doses of cortisone and corticotropin without production of significant undesirable effects.

However, a more difficult problem is presented by chronic diseases, in which prolonged therapy is required. All too often, the dose of cortisone or corticotropin which controls completely the clinical symptoms also produces significant undesirable effects when it is administered continuously for long periods. Most physicians[2,3,7,30] who have had extensive experience with the use of these hormones in rheumatoid arthritis, for example, do not attempt to maintain complete suppression of the clinical symptoms by means of continuous administration of large doses. The present trend is to use a dose of cortisone or corticotropin that gives reasonable but not necessarily complete control of the symptoms and that is small enough to avoid significant undesirable effects when given over a prolonged period. In the experience of Ward, Slocumb, Polley and Hench,[30] the average long-term maintenance dose can seldom exceed the limits of 50 mg. per day for menopausal or postmenopausal women, 62.5 mg. per day for other women and 87.5 mg. per day for men, without producing significant undesirable effects.

*Adrenal Suppression.*—Convincing evidence exists that the administration of cortisone leads to temporary suppression of function of the adrenal cortex.[4,12,14,15,28] The minimal dose and the shortest period of administration required to suppress the adrenal glands are uncertain. However, once suppression occurs, it probably is maintained by even relatively small doses and may even persist for several months after administration of cortisone is discontinued. During this period of adrenal cortical suppression, the patient's endogenous supply of cortisone or similar hormones is limited. While the patient may show no evidence of adrenal cortical insufficiency under ordinary circumstances during this period, unusual stress associated with such conditions as major injury, operative procedures, burns or acute severe illness may precipitate acute adrenal insufficiency. Consequently, during such episodes of stress occurring in this period of adrenal cortical suppression, not only must administration of cortisone be continued but the dose should be increased. In preparation for major surgical procedures in patients who have recently been given cortisone or who are receiving maintenance doses of cortisone, it is the practice at the Mayo Clinic

to give 200 mg. of cortisone intramuscularly forty-eight and twenty-four hours before operation and again on the morning of operation. After operation, the dose is reduced as rapidly as the condition of the patient will permit.

In the treatment of rheumatoid arthritis or other chronic diseases with cortisone, the following points in regard to regulation of the dose should be kept in mind:

1. The dose should be individualized to meet each patient's need and tolerance for cortisone, and the aim of treatment should be reasonable but not necessarily complete control of symptoms.

2. Multiple spaced doses should be utilized for oral administration of cortisone.

3. Sudden and drastic reduction of the dose should be avoided.

4. The patient who has been receiving maintenance doses of cortisone or in whom cortisone therapy has recently been discontinued will need additional supportive therapy during periods of stress.

I should like to caution against the use of these hormones in the treatment of undiagnosed illnesses. Because of the ability of cortisone and corticotropin to suppress or alter the symptoms of many diseases, it is not surprising that physicians are tempted to use these hormones prematurely when diagnosis is difficult and delayed. Patients with undiagnosed states of fatigue, with skeletal or muscular pain of unknown etiology, or with general malaise and low-grade fever of undetermined origin are among those who most often receive these hormones without benefit of a diagnosis. The premature use of these hormones not only is hazardous but may alter the clinical picture to such an extent that diagnosis is made even more difficult. In the latter case, the patient may be denied the benefit of more effective specific therapy. In light of the broad effects of cortisone and corticotropin, it would seem unjustified except in the most unusual circumstances to use these hormones before establishment of a diagnosis.

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*(Continued on Page 649)*

# THE ABUSE AND MISUSE OF ANTIBIOTICS

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WE ARE LIVING in an age in which both physicians and the general public have come to expect miracles of medicine and surgery, leaving little to the powers of Mother Nature. Rare is the physician who has not been urged to prescribe all manner of antibiotics for patients with fever or other equivocal evidence of infection. The pace of living and of medical practice is such that all too often the first question is not "What is the cause?" but rather "Should I take sulfa or penicillin?"

There can be little doubt that a considerable part of this attitude is the result of the barrage of publicity concerning the new "wonder drugs" loosed upon the layman and physician by popular "science" writers and pharmaceutical companies. Many a physician is loath to treat a respiratory infection without giving antibiotics lest he be subject to criticism by misinformed relatives of the patient. However, it is not the purpose of this paper to explore the reasons behind this trend but rather to point out some of the effects.

## Production and Cost of Antibiotics

As shown in Table I, the production of penicillin in the United States has increased astronomically in the ten years since its first use in human beings. The writer can remember the time when penicillin was so scarce and valuable that the urine of treated patients was saved and the penicillin therein extracted for other patients. Nine years ago penicillin sold for as much as $25.00 for a 10,000 unit ampule. At the moment one may purchase 500,000 units of a much more pure preparation for as little as $0.20. There has been a similar increase in production and decline in price of streptomycin since its introduction in 1945 (Table I). Production figures are not yet available for the "broad spectrum" antibiotics. There has been some reduction in their price, however.

TABLE I. PRODUCTION OF PENICILLIN AND STREPTOMYCIN IN THE UNITED STATES.*

| | *Year* | *Quantity* |
|---|---|---|
| Penicillin | 1942 | Enough for 100 patients |
| | 1949 | 8,000 billion U./mo. |
| | 1950 | 22,000 " " |
| | 1951 | 30,000 " " |
| | 1952 | 40,000 " " |
| Streptomycin | 1948 | 3,000,000 Gm./mo. |
| | 1949 | 7,000,000 " |
| | 1950 | 8,000,000 " |
| | 1951 | 10,000,000 " |

*Adapted from Welch and Lewis "Antibiotic Therapy."[4]

In Figure 1 are presented data indicating the monthly expenditure for four commonly used antibiotics in a 1000-bed general hospital during the past three years. One can see that during that period the total expenditure for antibiotics per month remained relatively stable. However, as new antibiotics came into frequent use, the amount of money expended for the other antibiotics declined. During this period the price of these antibiotics to this hospital remained quite constant. Therefore, the data give a fairly accurate idea of the changes in quantity of these antibiotics in use. They reflect the waxing and waning of enthusiasm of the physicians for new antibiotics.

## Untoward Results of Antibiotic Therapy

Aside from the inconvenience, loss of time and unnecessary expenditure of money, the use of antibiotics without strict indications is objectionable from several other points of view. These objections have received publicity in medical journals, but are important enough to bear reemphasis.

1. *False Sense of Security.*—Antibiotics are often administered simply to bolster the confidence of the patient, his relatives and his physician. All too often they are given in the absence of a definite diagnosis and even in the place of indicated diagnostic procedures. Every clinical

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pathologist and bacteriologist is aware of the difficulty which antibiotic therapy imposes upon subsequent attempts to isolate the causative organism in an infection.

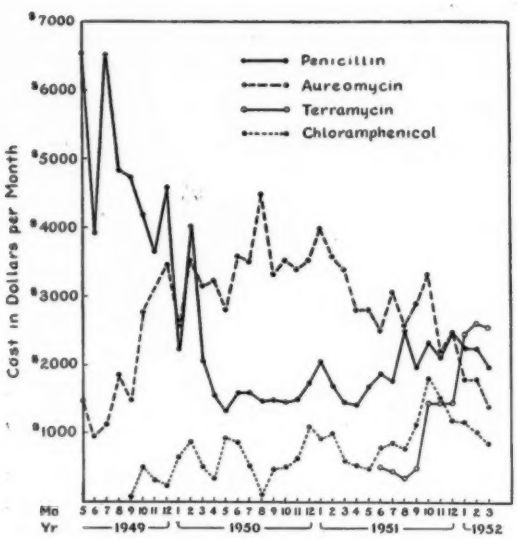


Fig. 1. Cost of antibiotics in a 1,000-bed general hospital.

The use of antibiotics may also give the false impression that everything is being done that can be done for an obscure illness. During the past year the author has had the opportunity to treat forty-four service men with vivax malaria contracted in Korea.[1] The first twenty-five patients were seen before there had been any publicity concerning the problem, either in the lay or medical press. Twenty per cent of this group had received penicillin prior to hospitalization. This was obviously largely due to the fact that the correct diagnosis had been made by the referring physician in only seven of the twenty-five patients and in none of those receiving penicillin. Smears of the peripheral blood eventually led to the correct diagnosis and treatment with effective antimalarial drugs.

2. *Development of Bacterial Resistance to Antibiotics.*—Widespread or indiscriminate use of antibiotics therapeutically, prophylactically or as food supplements may lead to a marked increase in tolerance of bacteria to those antibiotics. Presumably, the increase in antibiotic resistance results from the suppression of sensitive bacteria and selective proliferation of resistant variants arising by mutation. There can be no doubt that with such antibiotics as streptomycin the problem is a serious one. Coliform bacteria have been observed to undergo a 50,000-fold increase in resistance after only forty-eight hours of exposure to streptomycin. Similarly, many of the patients in tuberculosis sanitoria today harbor streptomycin-resistant tubercle bacilli. Time will tell whether the same phenomenon will be an important problem with isonicotinic acid hydrazide.

TABLE II. INCIDENCE OF RESISTANCE TO VARIOUS ANTIBIOTICS BY 155 STRAINS OF STAPHYLOCOCCI.

| *Antibiotic* | *Per Cent Resistant** |
|---|---|
| Penicillin | 54.8 |
| Terramycin | 27.1 |
| Aureomycin | 26.4 |
| Streptomycin | 20.6 |
| Chloramphenicol | 11.6 |
| Bacitracin | 7.1 |

*Resistance determined by paper disc-plate method.[2]
Antibiotic discs supplied by Difco Laboratories, Detroit, Michigan.

Antibiotic resistance has been a frequent problem in staphylococcic infections. Staphylococci seem peculiarly prone to develop resistant variants. There is evidence that staphylococci are becoming more frequently and more markedly resistant to penicillin year by year.[3] Recent studies in our own laboratory indicate that the incidence of resistance to a particular antibiotic correlates well with the amount of that antibiotic in use (Fig. 1 and Table II). The staphylococci used in the study summarized in Table II were all isolated from patients hospitalized at the Minneapolis Veterans Hospital during the period from July 1951 to April 1952. The 155 strains include all the staphylococci isolated regardless of source, coagulase reaction, pigment or hemolysin production. The sensitivity tests were all performed by the paper disc-plate method.[2] A sufficient number of strains have been tested for penicillin sensitivity using both the disc method and broth tube-dilution method to indicate that the disc method is reasonably accurate. It is generally agreed that the majority of strains of staphylococci are now resistant to penicillin; many are resistant to aureomycin, terramycin and streptomycin. All but a few are still sensitive to chloramphenicol and bacitracin.

3. *Side Effects and Hypersensitivity.*—Untoward side effects of antibiotics have received

considerable attention in the medical literature. Eighth nerve damage with streptomycin and neomycin and renal toxicity with bacitracin and polymyxin B are well-known entities. Urticaria and drug fever are commonly recorded manifestations of hypersensitivity to antibiotics. There are other less well-defined results of antibiotic therapy which may fall in this same sphere. They are illustrated by the two case reports which follow.

*Case 1.*—N.J.F., a white male truck driver, forty-three years old, was admitted to the hospital on February 20, 1950, for fusion of the left ankle. In 1944 he suffered a compound fracture of the lower end of the left tibia. This was followed by traumatic arthritis and recurrent phlebitis. In 1949 the left saphenous vein was ligated and stripped. At that time he was given procaine penicillin 300,000 units daily without reaction.

Physical examination revealed limited, painful motion of the left ankle. The skin of the ankle was discolored and edematous. On February 23, 1950, a left ankle fusion was done. Procaine penicillin (300,000 units daily) was given for one week prophylactically.

On March 17 he developed fever and pain in the ankle and by March 20 there was an obvious wound abscess. Aqueous penicillin G (150,000 units) was given intramuscularly every three hours for four doses on March 21. He was also given 250 mg. of aureomycin orally every four hours for three doses. The antibiotics were discontinued the following day because of fever, urticaria, severe crampy upper abdominal pain, nausea and vomiting. The abdomen was distended and roentgenograms revealed gas in the colon and small intestine. The leukocyte count was 23,400 with 84% neutrophiles and 2% eosinophiles. On March 24 he began to have diarrhea and passed several loose, bloody stools. Because of evidence of peritoneal irritation and his failure to improve with antihistaminic drugs and intestinal decompression by Miller-Abbott tube, a laparotomy was performed on March 27, 1950. There was more than 1000 cc. of clear yellow peritoneal fluid present. The jejunum and ileum were distended and edematous. Peyer's patches seemed enlarged and there was marked dilatation of the serosal blood vessels. Several ecchymoses were seen in the serosa. The mesenteric lymph nodes were only slightly enlarged. The colon appeared normal. The process was interpreted as an allergic enteritis.

The patient recovered quickly and was well by March 30. Benadryl was given during the postoperative period. On May 23, 1950, the ankle wound was incised and drained because of osteomyelitis. Aureomycin and chloramphenicol were given without event. Culture of the wound yielded penicillin-resistant staphylococci.

*Comment.*—This patient received procaine penicillin in 1949 and again late in Feb. 1950 without event. However, when given penicillin and aureomycin in March, 1950, he immediately developed drug fever, urticaria and an allergic enteritis with melena. Penicillin hypersensitivity seemed responsible since aureomycin was given later without reaction. Performance of antibiotic sensitivity tests upon a culture at the onset of the wound abscess would have prevented the therapeutic error.

*Case 2.*—D.A.P., twenty-two-year-old, male college student, was admitted to the hospital on Feb. 14, 1952. He had an upper respiratory infection beginning about Feb. 1, 1952. One week later he noted stiffness and swelling about the right temperomandibular joint. A physician denied that he had mumps and administered sodium salicylate. He continued to feel ill and had a fever. On Feb. 5 he took 300,000 units of penicillin and two tablets of a triple sulfonamide mixture every four hours. This was continued for three days without benefit. His right testicle then became swollen and tender. He was then given gantrisin and terramycin without improvement.

His past health had not been good. He was discharged from the Marine Corps in November, 1950, because of psychogenic gastrointestinal disturbances. He was immature and greatly dependent upon his mother. Aided by physicians and a friend employed as a detail man for a pharmaceutical firm, he became accustomed to the constant use of barbiturates. In addition, he used a variety of antibiotics in various forms with each of his frequent upper respiratory infections. He had suffered no side effects other than diarrhea attributed to aureomycin.

Physical examination showed a temperature of 99°F. and swelling, redness, tenderness and increased warmth of the right testicle. There were no other abnormalities.

Urinalysis revealed no pathologic changes. The hemoglobin was 16.6 Gm.% and leukocyte count 8,100 with 58% neutrophiles, 36% lymphocytes, 4% monocytes and 2% eosinophiles. The sedimentation rate was 13 mm. in 1 hour.

Chloramphenicol (500 mg.) was given orally every four hours and penicillin (200,000 units) every six hours. His temperature then rose to 101°F.; he complained of dyspnea with chest pain and began to cough up blood-streaked sputum. A chest roentgenogram showed bilateral hilar adenopathy. Bronchoscopy showed nothing other than a few flecks of blood. Smears of bronchial washings contained numerous yeast cells and mycelium; cultures yielded a non-pathogenic species of Candida (Monilia). Numerous sputum specimens showed the same yeast but no tubercle bacilli or other pathogens.

On the sixth hospital day, crepitant rales were heard at the base of the right lung and a roentgenogram showed an infiltrate in the right lower lobe and in the left upper lobe. On the ninth day a precordial gallop and a pleural friction rub at the right base were heard. The electrocardiograms revealed only nonspecific T wave changes. Penicillin and chloramphenicol were discontinued then since his fever, orchitis and hemoptysis continued unabated. His fever became septic, rising to 104° F. Because of increased fever and spreading pulmonary infiltrate, chloramphenicol (500 mg.) was given again every six hours from the tenth through the thirteenth

hospital day. A weeping, erythematous dermatitis of the penis and scrotum then developed. This plus continued fever, hemoptysis and spread of the pneumonitis to the upper lobe of the right lung prompted withdrawal of all antibiotics.

Biopsy of the right testicle showed chronic nonspecific inflammation without demonstrable bacteria, yeasts or fungi; culture of the testis and of scrapings of the scrotum both contained a Candida nonpathogenic for a rabbit and without the biochemical activity or spores of *Candida albicans*. Skin tests for tuberculosis, histoplasmosis, coccidioidomycosis and blastomycosis were negative.

Within forty-eight hours after all antibiotics were discontinued, the patient became afebrile. The hemoptysis ceased and his orchitis subsided. Furthermore, physical and roentgenologic evidences of pulmonary consolidation slowly resolved. By April 11, 1952, the only demonstrable chest abnormality was "fibrosis" and moderate hilar adenopathy. At the height of his illness the leukocyte count rose to 25,300 with 75 per cent neutrophiles and a sedimentation rate of 37 mm. in one hour. During convalescence the leukocyte count and sedimentation rate returned to normal but as many as 8 per cent eosinophils were seen in the peripheral blood. The patient was discharged apparently well April 11.

*Comment.*—The pathogenesis of this patient's illness is not entirely clear. The most likely probability is that he had a viral respiratory infection at the onset. Treatment with multiple antibacterial agents then suppressed the susceptible bacterial flora and allowed Candida to proliferate in the bronchi. The orchitis may have been the result of drug hypersensitivity or dissemination of the Candida; pathologic proof of the latter was not obtained though culture of the testicle yielded Candida (contamination from the skin?). The occurrence of hilar adenopathy and pulmonary consolidation suggested the diagnosis of sarcoidosis. However, all but the hilar adenopathy and the pneumonitis rapidly regressed soon after the antibiotics were discontinued. The occurrence of eosinophilia during recovery supports the thesis that antibiotic hypersensitivity played an important role in his illness. Several investigators have shown that a change occurs in the flora of the mouth and gut during treatment with aureomycin, terramycin and chloramphenicol leading to a predominance of resistant yeasts, staphylococci and Pseudomonas. Perhaps similar changes may occur occasionally in the bronchi and lead to dissemination of these organisms elsewhere in the body. This thesis seems to fit well with the known facts in this case. There was no evidence of a deficiency of any known vitamin.

### Summary and Conclusions

1. The astounding increase in production of antibiotics in this country in the last decade has led to a very desirable reduction in cost, but has also led to indiscriminant use by some people. This has had several undesirable effects.

2. One undesirable effect has been a false sense of security by reason of faith not justified by facts. This has led to use of antibiotics in some situations without good indications.

3. A serious hazard has been the rapid increase in prevalence of certain bacteria which are resistant to the antibiotics but are fully virulent.

4. Another important result has been the not infrequent conversion of a minor illness into a major disaster through the development of serious side effects, hypersensitivity states and alteration of the normal flora in the gastro-intestinal tract and elsewhere. The latter has been thought by some to lead to vitamin deficiencies but this remains unproved.

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## SOMETHING TO LOOK FOR IF YOU VISIT WASHINGTON

Some stories are news merely because they haven't been mentioned for sixty or seventy years. For example, the fact that the American Medical Association has its own memorial stone in the Washington Monument. It is at the 240-foot level of the 555-foot shaft. This was brought to our attention by Dr. Burt L. Davis of Palo Alto, Calif., who noticed the carved facing while walking down the stairs with his son. It is old and dusty, as are the records in which we are searching for more information.

# ABUSES OF A LOW SODIUM CONTENT DIET IN CARDIOVASCULAR DISEASE

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IN the past decade dietary restriction of sodium has been established as an adjunct to the therapeutic management of the cardiac patient who exhibits congestion. Schroeder pointed out that restriction of the intake of salt to a level less than the urinary output of chloride will decrease edema and that restriction of the intake of water alone is ineffectual.[14] As a consequence of use of diets low in sodium for congestive heart failure, adequate intake of water ordinarily can be permitted, and as a result of the alleviation of thirst and dehydration, the patient has been made more comfortable. Dietary restriction of salt also has made the task of obtaining and maintaining cardiac compensation easier and less time-consuming for the physician.

Use of diets low in sodium has been extended also to a place in the treatment of both essential and renal hypertension and in the management of fluid retention of nephritic, hepatic and hormonal origin.

The fact that this therapeutic tool can be applied by the patient himself as a part of his daily nutritional program makes it especially attractive to him. Many patients with cardiac and other diseases of organic or functional type are particularly receptive to the idea that the cause and cure of their malady are based on what they ingest.

Restriction of the intake of sodium and chloride for heart disease is a rational therapeutic measure only when the cardiac disease has progressed to the point of provoking renal mechanisms which cause retention of these electrolytes and water. Although controversial beliefs still exist, the concept is now widely accepted that edema in cardiac failure is caused by retention of salt and water secondary to the failure of the kidneys to excrete salt and water.

The fundamental initial physiologic disturbance in chronic congestive heart failure is the relative or absolute decrease in cardiac output. As a result of decreased cardiac output, there is a decrease in the renal plasma flow and in the rate of glomerular filtration.[11] According to Stead, tubular function in straightforward congestive failure remains good. As a result the reduced glomerular filtrate with its sodium chloride and water is more nearly completely reabsorbed than normally and thus is retained.[19] Undoubtedly hormonal and probably neurogenic influences are involved in this renal participation in the syndrome of congestive failure, but the actual mechanisms are not clear.

TABLE I. FORMS OF HEART DISEASE IN WHICH THE DIET OF LOW SODIUM CONTENT IS WITHOUT SPECIFIC INDICATION

| |
|---|
| I. Irritable heart syndrome |
| A. Extrasystolic arrhythmias |
| B. Paroxysmal tachycardias |
| C. Neurocirculatory asthenia |
| II. Valvular heart disease without congestive failure |
| A. Rheumatic |
| B. Syphilitic |
| C. Subacute bacterial endocarditis |
| III. Acute rheumatic fever without failure |
| IV. Coronary atherosclerosis with angina pectoris and without myocardial failure |
| V. Acute myocardial infarction without congestive failure |
| VI. Congenital cardiovascular anomalies without congestive failure |
| A. Cyanotic type |
| B. Acyanotic type |

## Heart Disease Without Congestive Failure

For heart disease which is not associated with sufficient failure to produce renal retention of salt and water, the diet low in sodium has no value. Not only is this diet unnecessary but it may be detrimental to the patient from the psychologic, nutritive, economic and occasionally the health standpoints. The prescription of a diet low in sodium for patients because of the therapeutic philosophy that if no good results, at least no harm has been done, is to be deplored. Restriction of the intake of salt for cardiac murmurs, thoracic pain, dyspnea of intrinsic pulmonary origin or edema due to peripheral venous or lymphatic disease in the absence of cardiac decompensation cannot be justified.

Examples of cardiac disturbance both functional and organic in which dietary restriction of salt has been needlessly utilized are listed in Table I.

In all these types of cardiac problems the low sodium diet will have no effect on the pathologic

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process responsible for the symptoms and signs. Unnecessary dietary restrictions may interfere with appetite and cause unassessable nutritional impairment particularly for the patient who is recovering from rheumatic fever or acute myocardial infarction.

Psychologic factors in the management of cardiac patients have assumed an important place in this era of newspaper and radio health propaganda. Restriction of sodium when unnecessary serves to emphasize constantly to the patient his malady and to superimpose anxiety and heart consciousness which may even be detrimental to his cardiac status as well as making him genuinely uncomfortable. Diets poor in sodium necessitate the purchase of some special food products and alsó individualized preparation of food. This imposes an economic factor of significant proportion particularly on the needy. Depletion of sodium and chloride induced by dietary restriction of salt alone is rarely seen, but may be a real hazard when combined with administration of ionic exchange resins and mercurial diuretics, particularly when renal disease is associated. This phase of the abuse of the low sodium diet will be discussed more fully later.

### Congestive Failure

In the presence of congestive heart failure of any type the low sodium diet can be abused in a quantitative way. Not all patients with congestive heart failure have disease of equal severity and consequently not all will require similarly rigid dietary management.[8]

In clinical practice low sodium diets which provide approximately 0.2 gm., 0.5 gm. and 2 gm. of sodium a day are in common usage. The diet providing 0.2 gm. of sodium a day is rarely indicated even for the most severe congestive failure. Frequently for the patient who has moderately severe congestive heart failure a diet providing 0.5 gm. of sodium can be replaced by the diet providing 2.0 gm. of sodium after compensation has been restored. When aggravating factors which have contributed to a break in cardiac compensation such as obesity, hyperthyroidism, strenuous occupation and inflammatory diseases have been removed, cardiac function may be restored sufficiently to make other than mild dietary restriction of sodium unnecessary. It is doubtful, however, whether an entirely free dietary regimen should ever be permitted the patient with organic heart disease who has once had frank congestive failure with cardiac edema.

### Hypertension

Current application of the low salt diet to the management of hypertensive vascular disease was stimulated by Kempner's successes with the rice diet.[7] Grollman and associates demonstrated that rigid restriction of sodium in a more liberal diet also was associated with reduction in the blood pressure of hypertensive rats and human beings.[4] This latter observation suggested that the efficacy of the rice diet lay in its low content of sodium. Later studies have indicated that the renal hemodynamics of hypertensive patients may be somewhat impaired during treatment with the low sodium and rice diets.[1,21]

Recently, Corcoran, Taylor and Page carefully studied a series of patients and found that marked dietary restriction of sodium produced favorable effects on only approximately a fourth of the patients with severe hypertension.[3] Their studies indicated that for the diet to be of value in the treatment of hypertension the intake of sodium must be restricted to 0.5 gm. or less daily and that this dietary regimen cannot be accepted as responsible for results obtained unless the urinary excretion of sodium is determined frequently. These authors also reported that treatment with restriction of sodium should be maintained four weeks to test the responsiveness of the patient to this form of therapy. Failure to see good results after this period is an indication that the restriction is probably useless and should be discontinued.

Abuse of the low sodium diet for hypertension has manifested itself in several ways:

1. The mere advice to the patient to "go easy on the salt" is a worthless measure since restriction of intake of sodium to any extent that is less than that rigidly imposed by the diets providing 0.2 gm. or 0.5 gm. of sodium or the rice diet is therapeutically ineffective.
2. Restriction of salt sometimes is continued for months or years in the absence of clear-cut satisfactory objective responsiveness and such continuation is not justifiable.
3. Use of the diet for the hypertensive patient with diminished renal functional capacity may be an abuse because of the danger of depletion of plasma electrolytes and derangement of the salt and water mechanism.

4. Probably the most frequent abuse occurs when sodium restriction is advised for the middle aged or older patient with nonprogressive essential hypertension of long standing. This type of patient often has an exacting and conscientious personality pattern and dietary restriction of salt which offers probably negligible benefit adds to a self-imposed discipline and creates anxiety and tension which are further stimuli to hypertension.

### The Syndrome of Salt Depletion

In addition to the relative abuses in the utilization of the diet of low sodium content which have been mentioned, a hazard of this regimen is the occasional occurrence of electrolyte depletion. The "low salt syndrome" has been found to occur when rigid restriction of salt alone is instituted, and also when ion exchange resin is used, particularly if there is significant renal deficiency.[9,10] Mercurial diuretics, when they have been administered frequently to the patient with congestive failure who is using a diet low in salt, however, have been held responsible most often for the electrolyte derangement in this syndrome.[2,6,17] Symptoms attributable to depletion of sodium and chloride also have been reported in cases of cirrhosis of the liver in which treatment included deprivation of salt and abdominal paracentesis.[5,13]

Schroeder[15] described this clinical syndrome in congestive failure. There is depression of the volume of urinary output and of urinary chloride associated with gain in weight, elevation of the concentration of nonprotein nitrogen in the blood and depression of the levels of plasma sodium and chloride. Coincident with these changes in water and electrolytes the patient becomes apathetic and lethargic and complains of anorexia, weakness and often of muscular cramps. The worsening of his general condition and retention of fluid are likely to encourage the physician to increase his efforts to produce diuresis and thereby further disarrange the plasma and renal electrolyte pattern.

Usually, the low salt syndrome develops after the patient with severe congestive heart failure of long standing has used a low salt diet, has further decreased the intake of sodium because of anorexia, and has been receiving frequent injections of mercurial diuretics. Such a patient has lost an excessive amount of chloride ion in the urine whereas the loss of sodium is not so great. This leads to a reduced concentration of chloride and an increase in plasma bicarbonate, that is, the laboratory picture of hypochloremic alkalosis.[16,18,20] At this point further mercurial diuretics are ineffective except to eliminate both chloride and sodium and thus also produce hyponatremia. The patient will present symptoms of the low salt syndrome described before. Continued rigid dietary restriction of sodium and chloride and their diuresis, as a result of administration of mercurials may lead to frank psychosis, coma and death.[2]

The treatment of choice for this situation is the restoration of the electrolytes to a more nearly normal state. Elevation of plasma sodium and chloride by their parenteral or oral administration will sometimes be associated with subjective improvement and responsiveness to mercurial diuretics.[2,15,20] Undoubtedly many patients who have been classified as having intractable and terminal irreversible congestive heart failure because of failure to respond to restriction of sodium and administration of mercurials actually have electrolyte depletion. Although in most such instances the severity of the cardiac disability militates against further compensation, some patients will respond again to well-conceived therapy. When hypochloremia is extreme in the absence of significant hyponatremia, use of ammonium chloride will correct the low level of serum chloride and will reduce the alkalosis.[16,20] Combined hyponatremia and hypochloremia require use of sodium chloride: either by intravenous injection of a hypertonic (3 to 5 per cent) solution or by mouth in the form of salt tablets. The proper amount of salt to administer may be determined by calculating the deficit in terms of milliequivalents and converting this amount into grams for replacement.[15] Oral intake of fluids should be restricted during therapy with hypertonic solution of salt in order to avoid any extracellular dilution. Infusion of isotonic solution of sodium chloride also cannot be expected to alter hyponatremia and hypochloremia significantly unless large amounts are given which may be hazardous for the patient with congestive failure.[15,20]

Certainly the low sodium diet is again an indicated and necessary measure for the patient who has severe congestive heart failure with peripheral edema after electrolyte equilibrium has been accomplished. Caution in the use of mercurial diuretics and frequent estimations to avoid retention of urea are essential in further management to avoid further plasma depletion of sodium and chloride.

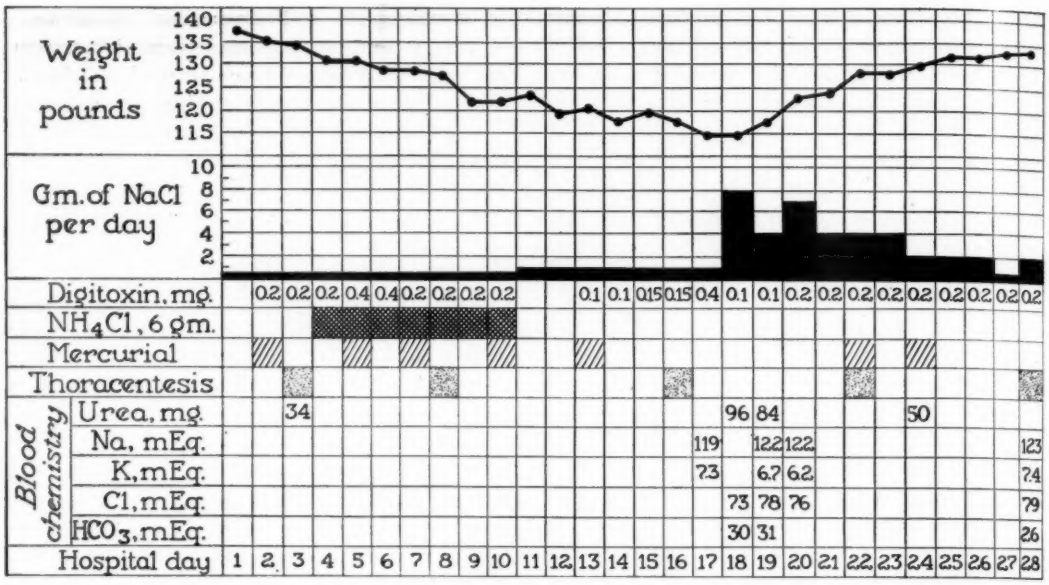


Fig. 1. Clinical and laboratory observations made in the case of a man forty-four years old, with mitral stenosis, who exhibited the low salt syndrome during his terminal illness.

Case 1 is an example of severe congestive cardiac failure and the low salt syndrome developing terminally.

*Case 1.*—A man, forty-four years old, was admitted to the hospital on March 3, 1951. He had known since 1940 that he had a heart murmur. Between the years of 1947 and 1950 he had five or six episodes which consisted of temperature to 103° or 104° F., chills and recurrent pleural effusion on the left side. During these years dyspnea became progressively more marked, and in October, 1950, edema appeared and albuminuria was noted.

On examination the patient presented the clinical picture of severe congestive heart failure. He was orthopneic and had distended veins of the neck, hepatomegaly, and marked peripheral and sacral edema. Apical systolic and diastolic murmurs were heard and cardiac enlargement was observed. Roentgenograms of the thorax showed a large heart of mitral configuration and bilateral pleural effusions. The electrocardiographic picture was consistent with the pattern of right ventricular hypertrophy. Albuminuria was graded 3 (on the basis of 1 to 4) and a few hyaline and granular casts were found in the voided urine.

The patient's course in the hospital was marked by severe dyspnea, orthopnea and evidence of fluid retention. Thoracentesis was necessary frequently. He complained of marked weakness, anorexia and drowsiness. Response to mercurial diuretics was poor.

Nausea, weakness and apathy were dramatically although temporarily improved on the eighteenth and nineteenth days in the hospital when extra sodium chloride was administered in the form of salt tablets and by intravenous infusions. This treatment, however, was associated with marked increase in retention of fluid and signs and symptoms secondary to increasing congestive failure. The patient died on the twenty-ninth day in the hospital. Necropsy confirmed the clinical diagnosis of severe mitral stenosis. Clinical and laboratory data collected during his hospital course are recorded in Figure 1.

This patient was treated vigorously with poor results for more than two weeks before the diagnosis of electrolyte depletion and associated azotemia was made. From an initial value of 34 mg. per 100 cc. of blood, the value for blood urea rose to 96 mg. at the time when serum sodium and plasma chloride were respectively 119 and 73.3 mEq. per liter. Mild hyperkalemia and increase in the carbon dioxide combining power (alkalosis) also were evident. Following therapy with sodium chloride these electrolyte values tended toward normal as noted in Figure 1. The cardiac lesion, however, was too severe to permit survival or even to allow restoration of plasma electrolytes to normal.

### Restriction of Sodium in Chronic Cor Pulmonale

In chronic cor pulmonale, right heart failure with cardiac edema is associated with respiratory acidosis secondary to pulmonary insufficiency. As a result of deficient ventilation carbon dioxide is

retained and the concentration of bicarbonate in the plasma is elevated. To compensate for retention of carbon dioxide in the blood, fixed base in the form of sodium ion must also be retained in the extracellular fluid.

TABLE II. PATIENT WITH COR PULMONALE

| | Day in Hospital | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10* | 11* | 12* |
| NaCl intake, gm. | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 5.0 | 0.5 | 0.5 |
| Digitoxin, mg. | | | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | | | |
| Mercurial, cc. | | | | | | 1 | | 1 | | | | |
| Phlebotomy, cc. | | | | | | | | | 300 | | | 300 |
| Urine, cc. | | | 200 | 300 | 320 | 300 | | 400 | 500 | 180 | 200 | 450 |
| Urea, mg. | | 56 | | | | | | | | | | |
| $Na^+$, mEq. | | 140 | | | | | | | | 138 | | |
| $K^+$, mEq. | | 5.8 | | | | | | | | 5.9 | | |
| $Cl^-$, mEq. | | 94.3 | | | | | | | | 85.7 | 86.8 | |
| $HCO_3$, mEq. | | 37 | | | | | | | | 27 | 38 | |
| Blood pH | | 7.25 | | | | | | | | 7.08 | 7.28 | |

*Clinical state:
Tenth day: collapse; critical condition.
Eleventh day: more alert and responsive.
Twelfth day: increasing edema.
Thirteenth day: died.

On theoretical grounds use of the low sodium diet particularly when combined with diuresis of sodium as a result of administration of mercurial diuretics may be a factor in upsetting the compensated respiratory acidosis. A few cases in which electrolyte disturbances were apparently disturbed by dietary restriction of salt and administration of mercurials have been encountered at the Mayo Clinic and undoubtedly other observers also have seen this syndrome.[12]

In Case 2 depletion of sodium was associated with severe symptoms.

*Case 2.**—This patient, a woman sixty-six years old, who had had severe kyphoscoliosis since childhood, was first admitted to the hospital in December, 1949, because of congestive heart failure associated with cyanosis. Her response was satisfactory to a program of digitalization, rest and a diet poor in salt. A second admission to the hospital was necessitated in June, 1950, when she had a severe respiratory infection. During that hospitalization an acute psychotic episode occurred which in retrospect was attributed in part to "oxygen poisoning." This paradoxical reaction occasionally develops when patients with severe pulmonary insufficiency are given oxygen in high concentrations.

The final admission of the patient on November 16, 1950, was precipitated by increasing dyspnea and cyanosis. Examination revealed severe respiratory difficulty, marked cyanosis, accentuated pulmonic second sound but no edema. She had 16.0 gm. of hemoglobin per 100 cc. of blood and 5,500,000 erythrocytes per cubic millimeter. Urinalysis disclosed nothing abnormal.

Significant electrocardiographic abnormalities were right axis deviation and inverted T waves in leads II and III. Her course was marked by continued cyanosis and dyspnea with weakness. She received only 0.5 gm. of sodium in her food although less was ingested because of anorexia. Mercurial diuretics were injected on the sixth and eighth days in the hospital. On the ninth and tenth days her condition became critical in that she was more dyspneic, stuporous and showed peripheral vascular collapse with hypotension and cold clammy skin. This phase was found to be associated with uncompensated respiratory acidosis (blood pH 7.08). The response to the intravenous administration of 500 cc. of normal saline solution was dramatic. She became alert and the blood pressure returned to normal.

Three days later the patient died as a result of increasing anoxia and congestive failure. Brief data concerning this patient's course are presented in Table II.

It would appear that renal conservation of sodium is necessary to compensate for the retention of bicarbonate in at least some cases of chronic cor pulmonale and that severe dietary restriction of sodium or diuresis may so deplete the body of necessary sodium that pH of the blood is lowered to dangerous and even fatal levels. This patient had responded previously in a satisfactory manner to moderate dietary restriction of salt in so far as the edema was concerned. In her terminal illness further depletion led to plasma acid-base imbalance, as recorded in Table II.

Rigid dietary restriction of sodium for chronic cor pulmonale particularly in the absence of marked edema may represent another little recognized abuse of this therapy. The management of the patient with pulmonary insufficiency and congestive heart failure is indeed difficult. Permitting a free diet leads to retention of fluid and more severe heart failure while withholding sodium and the use of mercurials may disrupt the electrolyte pattern which remains compensated only with difficulty. With present methods the

*This case is to be presented in greater detail as part of a paper being prepared by Dr. Myers.[12]

physician must feel his way along a middle pathway which may not be satisfactory in all cases.

## Summary

The diet low in sodium, although an extremely useful measure in the treatment of cardiovascular disorders, requires rational usage. It has no purpose in the treatment of heart disease unless there is evidence that cardiac output is reduced absolutely or relatively to the point at which renal mechanisms cause retention of salt and water and the syndrome of congestive heart failure is manifest. The insistence that patients with functional cardiac disturbances and with organic cardiac ailments who have never had a decompensation follow a low sodium diet is unwarranted and may be of nutritional, psychologic and economic detriment. The degree of restriction of sodium and chloride should be graduated for the patient depending on the severity of his congestive failure. When reversible cardiac loads have been removed, restriction of salt may be lessened accordingly.

Although hypertension may occasionally respond to a low sodium diet, its use is frequently abused by its being continued indefinitely for unresponsive patients, particularly when the degree of restriction is therapeutically inadequate.

A hazard of salt restriction especially when mercurial diuretics are frequently administered is the depletion of plasma electrolytes characterized clinically by what is known as "the low salt syndrome." Although this clinical state usually occurs in the terminal phase of congestive failure, it is sufficiently often reversible by restoration of plasma electrolytes to be considered in every patient whose condition deteriorates while being treated with a diet low in sodium. A return of the patient's responsiveness to mercurial diuretics at times may be produced by prompt therapy with hypertonic saline solution and sometimes with ammonium chloride.

Rigid dietary restriction of sodium and diuresis of sodium can disturb the compensated respiratory acidosis of chronic cor pulmonale and produce dangerous depression of pH of the blood.

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# THE USE OF METHANTHELINE BROMIDE (BANTHINE) IN PEPTIC ULCER AND OTHER GASTROINTESTINAL DISORDERS

## With Special Reference to its Abuses

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EVER SINCE the enthusiastic reports of Grimson and his co-workers,[3,4] Banthine has come to be widely used, especially in the treatment of peptic ulcer and many reports of its efficacy have appeared in the literature. In his original trials of the drug, in order to more clearly note its effect, Grimson used no other adjuncts such as diet, antacids, et cetera, in his treatment of peptic ulcer. While this procedure was justifiable and necessary in order to evaluate a new drug properly, it has had the unfortunate effect, in some circles, of creating the impression that prescribing Banthine is all that is necessary in the treatment of peptic ulcer. This conclusion was never intended by Grimson and his co-workers and subsequent studies have served to emphasize the fact that Banthine should be considered only as an adjunct to other fundamental methods of therapy.[1,2,6,7,8]

In order to understand the proper place of Banthine in present-day gastroenterological therapeutics, it is necessary to review, briefly, the information which has accumulated in regard to the effects of this drug on the gastro-intestinal tract. All are agreed that the fundamental effect of Banthine is to inhibit the acetyl-choline liberated at the post-ganglionic parasympathetic nerve endings, thereby blocking vagal impulses. In larger doses it blocks the transmission of impulses through autonomic ganglia as well. In the usual therapeutic doses, therefore, Banthine has an atropine-like action. The remarkable features of the Banthine effect are that the wanted atropine-like action on gastrointestinal motility and secretion is dominant, while the unwanted atropine-like actions such as tachycardia, flushing, cerebral stimulation and mydriasis are minimal, or absent. These are the features that make Banthine a more useful drug than atropine in gastroenterology.

McHardy et al[6] measured salivary secretion before and after Banthine and found a marked inhibition in 86 per cent of cases. In most, this lasted only about seventy-two hours. They found no effect on esophageal secretion. Cardiospasm was accentuated by Banthine; in fact, radiologically demonstrable cardiospasm was present in 18 per cent of 200 patients with duodenal ulcer on Banthine therapy as compared with only 3 per cent before Banthine was started.

All authors are agreed on the profound effect of Banthine on gastric motility. Balloon-kymograph, x-ray and gastroscopic studies have demonstrated the ineffective peristalsis, delayed emptying, and atony of the gastric wall. Most writers refer also to the diminution in the volume of gastric secretion following Banthine. McHardy et al[6] and Winklestein[8] dispute this. The decrease in titratable free hydrochloric acid in the gastric secretion following Banthine apparently has not been as uniformly demonstrated as the decrease in volume. In addition to its effect on gastric motility and volume of secretion, Wolf et al[1] have demonstrated a definite decrease in congestion and turgor and a thinning of the gastric rugae following Banthine.

All are agreed that Banthine accentuates pyloric obstruction and should not be used when this is present. If the obstruction is transient and due to spasm or edema, it should not be used until the obstruction has been relieved by other means.

Pancreatic secretion as measured in pancreatic fistulae has been shown to be definitely decreased by Banthine,[6] and there appears to be a definitely beneficial effect on acute pancreatitis and chronic recurring pancreatitis with calculosis, although we cannot by any means speak as yet of any cures. Biliary drainage has been shown by these same authors to be increased. Drainage from ileostomies as well as from colostomies at various levels are quite uniformly decreased.

Almy et al[5] state that Banthine inhibits the motility of all portions of the resting gastrointestinal tract. With the balloon-kymograph they have shown that 100 mgm. orally prevents the hypermotility of the sigmoid which usually follows the ingestion of foods and the subcutaneous administration of urecholine and morphine sulphate, but it only partially suppresses the sigmoid hyper-

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motility accompanying emotional tension during a disturbing interview. These authors as well as McHardy et al[6] speak of its clinical usefulness in some forms of hyperperistaltic diarrhea and in relief of intestinal pain. Spastic constipation, however, is not affected. The latter authors call attention to its lack of effect in various obstructive types of diarrhea and in chronic ulcerative colitis.

In addition to these actions which, in general, can be considered to have some clinical usefulness, there are side-effects which may at times make the use of Banthine uncomfortable for the patient or constitute definite contraindications to its use. The absolute contraindications can be stated as being: (1) bladder neck obstruction; (2) coronary insufficiency and cardiac decompensation; (3) glaucoma; (4) achalasia or cardiospasm; (5) pyloric obstruction, and (6) adynamic ileus. Bladder retention is usually thought of as occurring only in older men with enlarged prostates. It, however, has also occurred in women, probably due entirely to the induced atonicity of the bladder wall. Whether or not an undiscovered cicatricial urethritis could be a factor is difficult to say. Other side-effects such as visual disturbances, dryness of the mouth, and constipation are usually transient or so minor that they need not be given serious consideration. Very occasionally they may be distressing enough to the patient to warrant either decreasing the dose or discontinuing the drug entirely. On one occasion very severe dysphagia and pain along the esophagus developed which did not disappear until about five days after the discontinuance of the drug. Banthine should not be used in the immediate preoperative period as it will almost invariably lead to postoperative bladder retention.

It can now be stated that Banthine has been shown to be the most potent and useful antispasmodic agent yet developed. With special reference to its use in *duodenal* ulcer, most writers are agreed that it constitutes a valuable addition to our armamentarium if used together with other accepted methods of therapy. McHardy and his group[6] are the only writers I have encountered who state that their percentage of good results has been no greater with Banthine than without. Others agree that even in the so-called intractable cases, provided pyloric obstruction is not present, the addition of Banthine results in symptomatic relief and disappearance of the crater in the vast majority. It is still too early to say how permanent these results will be. Recurrences of ulcers while on therapy have been reported. In some of these, treatment has been inadequate. In general, the results are still on the positive side.

The results of therapy with Banthine in *gastric* ulcer have not been so convincing. A few patients seem to respond well, but, from all reports, the majority are very little if at all benefited. Excellent relief has been reported in a few cases of hyperacidity syndrome, marginal ulcers and peptic ulcers in hiatus hernia.[2]

The misuse and/or abuse of Banthine can probably be grouped under four main headings:

1. *Expecting the drug to accomplish more than our present experimental data would warrant.* Under this heading is included the tendency simply to hand the patient a prescription for Banthine and expecting thereby a cure for his ulcer. It must be remembered that, according to our present knowledge, the effect of Banthine on the course of duodenal ulcer perhaps is brought about entirely by its profound effect in suppressing gastric motility and its moderate effect in decreasing the volume of gastric secretion. It still behooves us to see that the patient obtains the needed rest, that his life be regulated so as to avoid tension and strife as far as possible, and that proper diet and, in certain cases, at least, antacids be administered so as to provide a medium which is conducive to the healing of the ulcer.

2. *Improper use of the drug.* It must be remembered that the effect of one dose of Banthine does not last longer than four to six hours, so that the drug must be administered at least every six hours throughout the twenty-four hour period, and especially at night when there is nothing in the stomach to buffer the effect of the acid peptic juice on the ulcer. This must be continued until there is evidence of complete healing of the ulcer. In other words, one tablet two or three times daily is not adequate. Complete therapeutic trial cannot be said to have been carried out until 100 mgm. (2 tablets) have been given every six hours. In some cases this may have to be increased to every four hours. Wolf states that during periods of stress it may be necessary to increase the dose temporarily. The prescribing of Banthine to be taken only as pain comes on cannot be condoned.

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# BLOOD GROUP FACTORS

## Part II. Rh Sensitization

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THE discovery of the Rh-Hr system of blood groups and the recognition of sensitization to these factors have constituted one of the important medical contributions of the past decade.

The general principles of intra-group sensitization were correctly elucidated by the early workers on Rh,[10,11,12,18] and in the intervening years these principles have been changed very little. Individuals who lack certain blood group antigents, if inoculated with them, may react to these substances as though they were foreign proteins. The initial exposure of the individual to the foreign blood factor produces no reaction but may stimulate the formation of antibodies. Once the antibodies have been produced, subsequent introduction into the blood stream of the specific blood antigen will produce untoward antigen-antibody reactions. Exposure of the body to foreign blood group antigens can be accomplished in either of two ways: (1) by the introduction of incompatible blood, either as transfusions or as subcutaneous, intramuscular or intraperitoneal injections, or (2) by pregnancy, in which foreign blood group antigens from the fetus are introduced into the mother by way of the placenta. First we shall consider sensitization produced by repeated transfusion.

### Repeated Blood Transfusions

If repeated transfusions of Rh-positive blood are given to an rh-negative recipient, that person is likely, sooner or later, to produce Rh antibodies. This antibody producing response of rh-negative persons to the Rh antigen shows considerable individual variation. Following such repeated transfusions, about 50 per cent or more of the recipients develop some degree of demonstrable sensitization,[4,12] whereas a small proportion fail to show any sensitization even after several transfusions. Inoculations of volunteers for the purpose of developing anti-sera is successful to some degree in the great majority of cases.[19] It seems clear that sensitization is very frequent after transfusion of Rh-positive D ($Rh_o$) blood to an rh-negative d ($Hr_o$) recipient. It can be concluded from this that every precaution must be taken to avoid the transfusion or injection of Rh-incompatible blood.

### Sensitization Due to Pregnancy

On the other hand, sensitization of rh-negative (cde) mothers by an Rh-positive fetus is relatively uncommon.[2,17] In one series of antibody studies[8] on almost 4,000 rh-negative women with Rh-positive husbands, the incidence of sensitization was 1 in 19. Even making appropriate allowance for pregnancies yielding rh-negative children and for first pregnancies (it generally requires at least one pregnancy to sensitize a mother), the estimated incidence of sensitization in this study still was not over 1 in 10. These observations suggest the moral obligation of everyone teaching the principles of Rh sensitization to point out (1) that transfusion or injection of Rh-incompatible blood results in a high frequency of sensitization, and (2) that pregnancy in rh-negative women produces sensitization on the average in only about 1 in 20 women.

This ratio does not apply, however, to rh-negative women who have received previous transfusions or injections of Rh-positive blood. Because of the high incidence of sensitization following such transfusions, these women may already be sensitized to the Rh antigen at the time of their first pregnancy. Before we had knowedge of the Rh factors, transfusions with incompatible Rh blood were unfortunately not uncommon. It is now well known that rh-negative women who have previously received a transfusion of Rh-positive blood are more than likely to produce affected babies in future pregnancies.[5,13] Women who might have given birth to several normal children may have all their chances of future normal childbearing destroyed by a transfusion or even an intramuscular injection of Rh-incompatible blood.[1] Intramuscular injection of unmatched blood into infants should be discontinued.

### Rh-Hr Factors

As discussed in Part I of this review, the Rh-Hr system consists of three factors. The Brit-

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TABLE I. COMMON GENOTYPES AND THEIR PERCENTAGE DISTRIBUTION AMONG AMERICAN WHITES.

| Genotype | Percentage (Approximately) |
|---|---|
| CDe/cde | 32 |
| CDe/CDe | 17 |
| cde/cde | 15 |
| CDe/cDE | 14 |
| cDE/cde | 12 |
| cDe/cde | 2 |
| cDE/cDE | 2 |
| CwDe/CDe | 1 |

All others less than 1% each and less than 5% total.

ish CDE system of nomenclature enables physicians to better visualize the relationship of the three Rh genes and their family of variants or allelomorphs. In order to understand the somewhat complex Rh-Hr nomenclature, it is essential for the physician to fix in his mind that the Rh "positive" element is expressed in the British nomenclature by the capital letter, e.g., C (rh′) D ($Rh_o$) and E (rh″), whereas the rh "negative" or Hr element is expressed by the corresponding small letter, e.g., c (hr′), d ($Hr_o$) and e (hr″). He should have available in his library or office desk the table of frequencies for at least the most common of the different Rh patterns (genotypes) (Table I).

### Sensitization to Rh-Hr

The most commonly occuring Rh sensitization is in d ($Hr_o$) women exposed to D ($Rh_o$) antigen. From Table I it can be seen that the complete genotype of the great majority of these d ($Hr_o$) women is cde/cde. They are, therefore, rh-negative not only to D($Rh_o$) but also to the other two specificities of the Rh factor. Sensitization of C (rh′) negative and E (rh″) negative individuals to the corresponding positive C and E factors occurs frequently in completely rh-negative individuals (genotype cde/cde).

Since approximately 85 per cent of individuals are positive to D ($Rh_o$), 60 per cent are positive to C and 15 per cent are positive to E (Table I), it follows, therefore, that 85 per cent of cde/cde women will have husbands positive to D, and, in addition, about half of these husbands will be positive also to C and about one-sixth will be positive also to E. It can be seen, therefore, that commonly cde/cde mothers are exposed to multiple antigens, e.g., D plus C (CD) or D plus E (DE), and may form several antibodies simultaneously (Table II).

Sensitization of rh-negative (cde/cde) individuals is the most common, but many other types of sensitization do occur. In all cases, the same principle holds: a person is sensitized to a blood factor which he does not possess—homozygous c (hr′) individuals can be sensitized to C (rh′); C (rh′) to c (hr′); d ($Hr_o$) to D ($Rh_o$); D ($Rh_o$) to d ($Hr_o$); e (hr″) to E (rh″); and E (rh″) to e (hr″). Furthermore, all of the more recently discovered Rh allelomorphs $C^w$, $C^u$, $c^v$, and $D^u$ and the other blood factors, such as the MN, Kell, Lutheran, Duffy, Kidd and the Lewis, may be implicated in the same way. In fact, most of the Rh allelomorphs and most of the other blood group factors were discovered because of sensitization by multiple transfusions or pregnancy. However, the susceptibility to such sensitization varies tremendously and appears to depend both upon the antigen involved and upon the individual. In the case of some antigens the susceptibility is so slight as to be almost non-existent. The reason for such variation is susceptibility to the various blood group antigens is not entirely clear.

As previously stated, the most susceptible to sensitization are d ($Hr_o$) individuals exposed to D ($Rh_o$). However, in pregnancy, this most common form of sensitization occurs only in about one in twenty exposures. Almost equally susceptible is a cd ($Hr_o'$) individual exposed to CD ($Rh_o'$) resulting in sensitization to both C (rh′) and D ($Rh_o$). Curiously a cd ($Hr_o'$) or a cD individual exposed to CD ($Rh_o'$) rarely develops sensitization to C (rh′) only. Sensitization to E is uncommon and even more rare is sensitization of C or E individuals to the negative C (c) or negative E (e). The most striking example of apparent contradiction is in the d-D relationship. As stated above, a d($Hr_o$) person is relatively susceptible to sensitization by the D ($Rh_o$) antigen but a D ($Rh_o$) person is extremely resistant to sensitization by the d ($Hr_o$) antigen. Only three instances have been reported in the entire literature.[6,7,9]

Physicians often ask the question, "How can an Rh-positive woman become sensitized?" There are three ways in which this occurs. In the determination of Rh, the Rh antiserum used as a screening serum is an anti-D (anti-$Rh_o$) serum. This is the correct serum to use since bloods negative to this serum almost always (about 88 per cent) have the genotype cde/cde, that is, they are negative to all Rh specificities. However, bloods positive to this anti-D serum often are

CDe, cDE, or cDe, and therefore are negative to C (rh′) or E (rh″) or both, even though they are positive to D ($Rh_o$). Occasionally as stated previously some of these women positive to D ($Rh_o$) but negative to C (rh′) or E (rh″) can develop sensitization to C (rh′) or E (rh″).

Another mode of sensitization is even more uncommon but does occur. The individual positive to any or all of the three specificities of Rh, for example, can become sensitized to the c (hr′) or e (hr″) factors and presumably very rarely to the d ($Hr_o$). This is the so-called Hr sensitization.

Finally, the Rh-positive individual may be sensitized by pregnancy or by transfusions involving blood factors other than the Rh, such as the A, B, Kell, Duffy, Lutheran or others.

Table II lists various combinations of Rh genotypes as examples to illustrate possible Rh incompatabilities and the antibodies which might be formed. The table is arranged in the approximate order of the susceptibility to sensitization.

TABLE II. EXAMPLES OF RH INCOMPATIBILITIES

| Mother or Recipient | Fetus or Donor | Antibody Formed | Frequency |
|---|---|---|---|
| cde/cde | CDe/CDe or CDe/cde | Anti-D or Anti-D & Anti C | Common |
| cde/cde | cDE/cde | Anti-D or Anti-D & Anti E | Common |
| cDE/cDE | CDe/cde | Anti-C | Rare |
| cde/cde | cDE/cde | Anti-E | Rare |
| CDe/CDe | cde/cde | Anti-c | Rare |
| cDE/cDE | cde/cde | Anti-e | Rare |
| CDe/CDe | cde/cde | Anti-d | Extremely rare |

### Laboratory Reports

When sensitization has occurred and antibodies are present, it is customary to measure the concentration of the antibody in terms of titer, i.e., the number of times the serum can be diluted and still produce visible evidence of agglutination. Immunologists often express not only the titer but the strength of the agglutination of each dilution. This is an expression of the degree of clumping and is of minor significance to clinicians. However, if a case is to be reported in the literature the inclusion of the expression is worth while. An example of a complete expression is "titer, 1:32," followed by the designation of the degree of clumping in each dilution: "33321000," which indicates 3-plus agglutination in the first tube or 1:2 dilution of serum, 3-plus in the second or 1:4 dilution and so on.

As stated in Part I of this review, the study of rh-negative mothers should include a determination of the father's genotype. If the father is heterozygous Rh positive and therefore carries also an rh-negative (Hr) gene, half of the children can be rh negative. If he is homozygous Rh positive, all of the children will be Rh positive.

A typical example of a report of a complete study of an rh-negative mother, disregarding for the time being the albumin and Coombs' titrations, is as follows:

"Mrs. X is rh negative (cde/cde)and Mr. X is Rh positive to both C (rh′) and D ($Rh_o$) and is c (hr′) positive and is therefore heterozygous to C (rh′). His most likely genotype is CDe/cde, and if this is so, there is an even chance that children born to this union will be rh negative and therefore normal so far as Rh incompatibility is concerned.

"The serum of Mrs. X shows that she is sensitized to both the D ($Rh_o$) and C (rh′). The anti-D titer is 1:32; 33321000, and the anti-C titer is 1:4; 21000000."

With only minor variations, the above illustration is typical of many reports. In many cases the father's genotype will be CDe/CDe, in which case he is homozygous and all the children will be Rh positive. Or, his genotype may be cDE/cde in which case the rh-negative mother may be sensitized to E (rh″) as well as D ($Rh_o$).

### Modes of Action of Rh Antibodies

It is now well known that there are several types of Rh antibodies. These are identified by differences in their mode of action upon the specific antigen (Rh-positive red cells) when suspended in different media. The three types of antibodies for which tests are usually made are commonly called "saline," "albumin" and "Coombs" antibodies.

Originally the accepted method of carrying out a crossmatching of blood was to use a saline suspension of donor's red cells mixed with equal parts of the recipient's serum. It was to be expected that this same method would be used in the earliest Rh studies. Obviously the first type of antibody to be identified was therefore the saline antibody. Many instances of Rh sensitization were demonstrated by this method. But frequently negative mothers, unquestionably sensitized because they gave birth to erythroblastotic babies,

did not have antibodies demonstrable by this method. Many physicians can recall in the early days of Rh studies patients who, according to laboratory tests, showed no evidence of sensitization but who, nevertheless, delivered babies obviously afflicted with erythroblastosis. Occasionally, too, a recipient of a "perfectly cross-matched" transfusion died of a hemolytic reaction.

Laboratory workers soon modified their methods. By substituting for saline either human serum or a concentrated solution of albumin in making the suspension of red cells, many more cases of sensitization were demonstrated. This high protein method, developed originally for study of Rh antibodies, has now been included in transfusion techniques and is today the accepted procedure in all crossmatching of bloods for transfusion. This method is not only a more sensitive procedure but it has uncovered a new type of antibody. Many studies seem to show that the two antibodies are different both in chemical structure and biologic activities. The most easily demonstrated difference between the two antibodies is that one is active in a saline medium and the other requires an albumin medium; hence the terms saline and albumin antibodies.

An incidental characteristic of the albumin antibody is worthy of mention because this property yielded the term "blocking antibody," which appears to be so firmly fixed in the Rh literature. Albumin antibody, if mixed with Rh-positive red cells suspended in saline, cannot agglutinate them, but apparently this antibody adheres to and coats and blocks the cells in some way so that they no longer can be agglutinated, as they otherwise should be, by saline antibodies; hence the term, blocking antibody. Another term synonymous with albumin antibody or blocking antibody is "incomplete antibody." A term employed as synonymous with saline antibody is "agglutinating antibody." The serum sold commercially as "test-tube" serum is a saline antibody and that which is sold as "slide" serum is an albumin antibody.

Up to this point have been mentioned only saline and albumin (sometimes called blocking) antibodies.

In studies on evidence of pathogenesis of erythroblastosis, it has been found that the anti-human, globulin serum tests of Coombs, Mourant and Race[3] is an important serological adjunct to the investigation of immunization whether by pregnancy or transfusion.

This test is now widely used in general laboratory work. Coombs postulated that if proper red cells (antigen) are mixed with corresponding antibody, the antibody would adhere to the surface of the red cells even if agglutination did not occur. Since antibodies are modified globulins, it follows that the red cells exposed to the antibody should now be coated with a layer of the modified human globulin. Coombs prepared an anti-human globulin serum by injecting rabbits with human globulin. When he added this anti-human globulin rabbit serum (now known as Coombs' serum) to the treated red cells coated with human globulin, agglutination promptly occurred.

The Coombs test gives a positive reaction for any type of antibody that fixes itself to red cells. Sensitized mothers give a positive reaction regardless of whether the antigen involved is the Rh factor or one of the others, such as the Duffy, Lutheran, Kidd, Lewis or others, providing (and this is a big technical problem in small laboratories) that proper test cells are available. Antibodies of unknown origin which fix themselves to red cells causing hemolysis and thereby producing hemolytic anemias can be demonstrated by the test. Transfusion reactions due to weak antibodies not demonstrated even by the improved methods of cross-matching may be identified by the Coombs test. Erythroblastosis can be differentiated from other types of anemias and jaundice of the newborn by means of the test. It is very probable that all of the possibilities of the test have not yet been explored.

It is common practice in Rh laboratories to do all three types of tests, namely, saline agglutinating, albumin agglutinating and Coombs, on every specimen for which Rh antibody titrations are indicated. The titer of these antibodies follows a fairly consistent pattern. Both the albumin titration and the Coombs titration demonstrate not only their own specific antibody but also all of the saline antibody so that the values of each of these two titers should be at least equal to the saline titer; for example: saline 1:64, albumin 1:64. Coombs 1:64. Not infrequently the saline antibody is relatively decreased or disappears; for example: saline nil, albumin 1:64, Coombs 1:64. Rarely both saline and albumin antibodies are low or absent and only the Coombs titer is present; for example: saline nil, albumin 1:16, Coombs 1:64. Occasionally the Coombs titer appears to be lower than the others. This probably is due to

technical errors. As will be discussed later, the relative and not the absolute levels of these titers may be of some clinical significance.

The determination of sensitization to the various allelomorphs of the Rh system or to the other blood group antigens may be a long and tedious process. Study of a patient for one of the uncommon types of sensitization consists of setting up the serum against a large "panel" of known red cells. Some of these studies take several months to complete. To do such studies, the worker must have available an adequate "panel" of known sera and test cells. To assure the availability of known test cells and in view of the fact that cells are perishable, the worker must have at hand a list of people of selected groups who can donate of their blood as it is needed. A complication of this procedure comes from the fact that some genotypes are rare in the general population. Obviously these are not procedures one can request of the average hospital laboratory. Even in a laboratory devoted exclusively to sensitization studies such mass studies are not possible as routine procedures but rather come in the category of research. Such studies are carried out only when the usual routine tests are negative and the history given to the laboratory indicates that definite maternal sensitization or a true hemolytic transfusion reaction has occurred.

### Routine Rh Studies

Physicians commonly ask: "What program of Rh studies should be routinely carried out in obstetrical practice?" It is difficult to recommend a program equally acceptable to all physicians. Some physicians prefer to study each individual baby for evidence of erythroblastosis and to carry out maternal Rh studies only in selected cases. Many physicians request of the Rh laboratory tests to determine the Rh group of all pregnant patients and tests on the serum of rh-negative ones during pregnancy as a routine to detect as early as possible the development of sensitization to Rh. At least two determinations for Rh antibodies are usually called for: one at the time of the woman's first appearance at the physician's office or the antenatal clinic; the other about six weeks to a month before the expected date of delivery. Other physicians request antibody determinations at the time of the first visit of the rh-negative woman and then every thirty days from the fifth or sixth month of pregnancy until term. The rationale for this early test is that the finding of antibody early in pregnancy indicates that the woman had become sensitized by an exposure to the antigen at some time previous to the current pregnancy. Antibodies resulting from an initial sensitization due to the current pregnancy are seldom detectable before the fifth month. The following outline presents a sequence which can be modified by physicians to suit their own needs.

I. The first time the expectant mother presents herself for examination, take a specimen of blood for Rh determination.
   1. If blood is found to be Rh positive, proceed no further unless there is history of previous erythroblastotic babies. In these rare instances arrange for special studies (ABO, Rh subgroups, MN, Duffy, Kell, et cetera).
   2. If blood is rh negative, proceed to step II.

II. If blood of expectant mother is rh negative, take specimen of blood from husband for Rh determination:
   1. If husband's blood is rh negative, proceed no further.
   2. If husband's blood is Rh positive, determine whether he is homozygous or heterozygous, and proceed to step III.

III. If husband is Rh positive, take specimen of wife's blood to be tested for presence and concentration of Rh antibodies. If—
   1. Wife is Gravida 1 and antibodies are absent, send another specimen of her blood to laboratory at about the thirty-fourth week of pregnancy for antibody titration.*
   2. Wife is Gravida 1 and antibodies are present, it likely means that she has been previously exposed to the Rh antigen by transfusion, by intramuscular inoculation of blood or by earlier unrecorded pregnancy.** Send specimen of her blood to laboratory at sixth and eighth months of pregnancy for confirmation of the sensitization.
   3. Wife is multipara with normal prior babies and antibodies are absent, send specimen of her blood to laboratory at end of fifth, seventh and eighth months of pregnancy for further antibody titrations.***

*The statement that hemolytic disease of the newborn is rare in first pregnancies does not apply to women who have received previous transfusions or intramuscular injections of blood even in infancy. They may already be sensitized to the Rh antigen at the onset of their first pregnancy. It is now known that rh-negative women who have previously received any transfusions of Rh-positive blood are more likely than not to produce an affected child in any subsequent pregnancy.[5,13]

**It must be remembered that a pregnancy which terminates in an abortion, say at ten to twelve weeks, may be enough to sensitize a woman. Women who claim to be pregnant for the first time may be overlooking miscarriages manifested only by missed periods.[14]

***It is very important to be forewarned of the first erythroblastotic baby. This one probably can be saved and may be the last viable child of this woman.

4. Wife is multipara with prior erythroblastotic babies and,
   (a) husband is heterozygous, send blood for antibody studies at fifth, seventh and eighth months. A stationary titer indicates an rh-negative baby which should be normal.
   (b) husband is homozygous, all the children will be positive and the level of the antibody is of little value. Send her blood for study according to the individual circumstances: for the record or for academic interest. Blood from highly sensitized women is needed desperately for processing into diagnostic sera.

### Interpretation of Laboratory Results

The interpretation of the degree of Rh antibody titer in the serum from the pregnant woman is indeed difficult. Our own findings convince us that there is little correlation between antibody titer as such in the mother's serum and the severity of symptoms of hemolytic disease in the newborn. The titer often shows little change during pregnancy even when there is an Rh-positive fetus *in utero*. Then again, it happens that there may be a small increase in the titer of the Rh antibody even though the fetus *in utero* is rh negative. If, however, the titer of antibody increases markedly, say twentyfold or more, it can be considered likely that the infant *in utero* is Rh positive.

The fluctuations in the Rh antibody titer are not always a safe guide to judge the prognosis to the baby. It is not altogether clear why this should be so. Quite likely the titer represents to some extent the amount of antibody present in excess of that absorbed by the fetus. One woman may form only small or moderate amounts of antibody but if the baby absorbs little or none, the antibody accumulates in the mother's circulation and produces a rising titer. Another woman may produce larger amounts of antibody which is largely absorbed by the fetus. In such a woman antibody is being withdrawn from her circulation and the titer may rise only slightly, remain stationary or actually fall. Often the titer falls sharply late in pregnancy, probably because the increased fetal volume absorbs large amounts of the available antibody. Generally speaking, however, a consistently high titer—and especially a rising titer—often portends a grave prognosis.

Perhaps some reliance might be placed upon the relative values of the saline and albumin antibody titers. The physician need not concern himself with the complex and still uncertain physicochemical differences between the two antibodies. Suffice it to say that there is evidence to indicate that the earlier and presumably less severe stages of sensitization produce a higher ratio of saline antibody relative to the albumin type. In later and presumably in the more severe stages, the saline antibody decreases or disappears and the albumin antibody titer is relatively high. In general, one would expect a better prognosis if the titer is "saline 1:64, albumin 1:64, Coombs 1:64" than if the titer is "saline nil, albumin 1:64, Coombs 1:64."

The time during the gestation period in which antibody appears seems also to be important. Generally speaking, the earlier in pregnancy that the mother becomes sensitized, the graver the prognosis for the infant.

By far the most important guide in judging the prognosis for the unborn child is the mother's past record. Sensitization of the Rh type is a progressive process. Once a mother has reached the stage where the fetus is critically affected, the outlook for future normal Rh-positive children is very poor. For this reason, it is extremely important that erythroblastosis of moderate degree be promptly recognized and actively treated. It is very probable that this moderately ill child is the last Rh-positive child of this mother which can be saved.

In cases of these highly sensitized women, the homozygous or heterozygous state of the husband becomes important (see item III-4 of the above suggested outline for prenatal studies). Because of the reciprocal relationship of Rh and Hr types, the determination of Hr becomes an important laboratory adjunct in prognosticating, within limits, the chances of producing Rh-positive and therefore erythroblastotic babies or rh-negative and therefore normal offspring in future pregnancies in families where congenital hemolytic disease has occurred. However, since at present the available supply of Hr antiserum is limited to anti-c (anti-hr′) only, the clinical application of the Hr factor must be restricted at present to testing directly for homozygosity and heterozygosity of types CDe ($Rh_1$) and Cde (rh′) individuals. Through population studies, however, with suitable antisera, it has been possible to determine the frequency of gene arrangements on chromosomes and the incidence of the Rh and Hr types. From tables that have been constructed, e.g. Table I (abbreviated form), it is possible for the labora-

tory worker to calculate the chances of a man being homozygous or heterozygous Rh positive in Rh types where the anti-c (anti-hr') serum cannot prove it directly; and therefore predict the chances that a sensitized mother would have of producing normal offspring fathered by her Rh-positive husband.

### Laboratory Tests on Infants

The direct Coombs test is one which is of proven value at this time. It requires a minimum of equipment and results are obtained in about fifteen minutes. The application of Coombs serum to cord erythrocytes offers a means of differential diagnosis between erythroblastosis and such confusing conditions as other types of jaundice and anemia of the newborn.

Although the cord is a convenient source of blood for laboratory study, there is danger of contamination by mucus. The cord should not be squeezed unnecessarily during the collection of the blood. Rh tests, grouping, and Coombs tests on cord blood are reliable. Hemoglobin determination, icterus, and bilirubin studies are distorted by clotting, hemolysis and contamination by mucus. These should be confirmed by study of peripheral blood.

The laboratory tests ordinarily available to pediatricians are as follows:

I. Rapid centrifugation of cord blood collected into a dry tube containing oxalate or heparin so that supernatant plasma may be examined grossly for presence of icterus.
II. Slide test for Rh to determine rapidly Rh type of infant.
III. If infant is Rh positive, direct Coombs test on red blood cells of infant to determine if cells are coated with Rh antibody.
IV. Hemoglobin determination on infant's blood.
V. Other less urgent tests:
   1. Erythrocyte count and differential.
   2. Rh antibody titration on blood serum from infant.
   3. Bilirubin content more accurately determined.

### Preparation of Transfusions

Several of the newer studies on blood group antigens and antibodies find ready application in transfusion work.

The principle of the albumin (high protein) method of cross-matching of blood is unquestionably sound. Workers are continually searching for improvements in this method. Just as the albumin method of Rh antibody study has demonstrated many more cases of sensitization than was possible by the older saline method, so this same method applied to cross-matching of blood is far more reliable than the original saline method. The procedure is recommended without reservation, but it may be expected that refinements may be forthcoming.

The use of the Coombs test as an adjunct to the cross-matching of blood is proving of considerable value. As already discussed, saline and albumin types of antibodies may disappear or be of such low titer that they are almost imperceptible, yet the Coombs test can be strongly positive. Therefore, in a patient who is having reactions to transfusions, the next transfusion should be cross-matched by the albumin method, and if this is negative, the cross-matching should be still further studied by means of the Coombs test. The same precaution can be followed in preparing transfusions for women who have borne erythroblastotic babies or in patients who have had many prior transfusions.

The selection of rh-negative blood for sensitized rh-negative recipients should be done with exceptional caution. Since laboratories ordinarily have no knowledge of the patient's prior clinical record, the physician has the obligation to warn the laboratory; or better yet, the laboratory should regard all rh-negative patients as dangerous recipients.

Patients negative to the anti-D serum generally have the genotype cde/cde and as already stated are often sensitized to C or E as well as D. Therefore, the blood administered to rh-negative patients must be tested not only with anti-D serum, but also with anti-C and anti-E serum. Up to 2.42 per cent of the population have the genotype Cde/cde[20] and up to 1.3 per cent have the genotype cdE/cde[15] (depending on the racial distribution in the population).

The problem, however, is even more complex. In about 1.6 per cent of the population the allelomorph $D^u$ reacts weakly or not at all with anti-D serum,[16] and many individuals having this $D^u$ variant are typed as rh negative (cde). Such mistyped blood given to sensitized cde individuals can produce serious reactions. Generally the cross-matching, if done by the high protein method, should give some suspicion of incompatibility. If there is any question regarding the cross-matching, or, as stated above, if the recipient is known to be sensitized, the extra precaution of a Coombs test is indicated.

**Summary**

1. The basic principle of blood group sensitization has been modified very little since the initial work on the Rh factor. Individuals inoculated with blood factors which they themselves do not possess may react to them as though they were a foreign antigen.

2. Rh-negative (d) individuals given positive blood by transfusion or injection develop sensitization in most instances. On the other hand, sensitization by pregnancy in rh-negative individual occurs in only 5 per cent of the cases. An injudicious transfusion or injection of Rh-positive blood into an rh-negative woman may militate against the possibility of her ever giving birth to normal babies.

3. The Rh allelomorphs other than D and various other blood factors more recently discovered can cause sensitization, but there is marked variation in the incidence of sensitization to the various factors. Anti-C and anti-E sensitization are relatively common but only when combined with anti-D sensitization. The other allelomorphs and blood group antigens cause sensitization only occasionally. These latter factors do not need to be investigated in routine transfusion or Rh work but must be investigated when the usual causes of erythroblastosis and hemolytic transfusion reactions have been excluded.

4. Rh antibodies are of three types: saline, albumin and Coombs. The saline antibody receives its name because it will agglutinate red cells suspended in saline. The albumin antibody will agglutinate red cells only if they are suspended in an albumin medium. The Coombs test, which identifies the Coombs antibody, is a very valuable procedure applicable to many other types of laboratory studies. All its possibilities still may not have been developed.

5. Routine Rh work on obstetrical patients usually involves study of the D-d factors only. If, however, sensitization is definitely known to be present, as indicated by an erythroblastotic baby, and is not accounted for by D-d incompatibility, other blood factors must be investigated. Such studies may be quite involved.

6. A complete Rh study of an rh-negative woman includes tests for the three types of antibodies, titration of each, tests for coincident C or E antibodies, and the genotype determination of the husband to identify his homozygous or heterozygous state.

7. A sequence of Rh studies depending upon the parity of the mother and her previous clinical record is presented.

8. Emphasis is put upon identifying the first appearance of sensitization during the child-bearing period. It is believed that the one or two pregnancies in which the sensitization cycle is just starting may yield mildly affected children which can be saved by proper treatment.

9. Antibody studies in rh-negative women with advance sensitization is of value only if the husband is heterozygous and rh-negative children are therefore possible. The Rh status of the unborn infant can be forecast by such studies with acceptable accuracy.

10. Prognosis should not be based solely upon levels of Rh-antibody titer. Such levels probably represent the excess of antibody above that absorbed by the fetus and do not necessarily measure the amount actually combining with the infant's tissues. However, the relative amounts of saline and albumin antibody may be of prognostic value. The saline antibody appears to be less harmful, and the prognosis is better if this type predominates. The time during pregnancy at which sensitization occurs appears to have prognostic importance. The best prognostic guide is the mother's past history. Rh sensitization is progressive and once a mother has reached the stage of advanced sensitization, the chances for further normal children are almost non-existent unless the father is heterozygous and the next child is rh negative.

11. An increasing amount of the data collected by the Rh worker is being applied to general transfusion work. An example at point is the high protein method of cross-matching which is now the accepted method in many laboratories. The significance of the $D^u$ allelomorph is another example. This allelomorph often gives a weak or negative reaction to anti-D sera. Such a $D^u$ blood is often grouped as rh negative (d) and if transfused into a sensitized cde patient may give a serious reaction. The Coombs test may be used as an adjunct to the cross-matching of blood for recipients who have received many transfusions or for rh-negative women known to have borne erythroblastotic babies.

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# AMNIOTIC FLUID EMBOLISM

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THE following case is typical of the relatively rare condition known as amniotic fluid embolism. The case is of special interest because it contributes to our understanding of the mechanism of this obstetrical accident.

## Case Report

The patient was a gravida 4, with two living children. One child had died during delivery because of a prolapsed cord and breech presentation. In 1947 the patient apparently had an early abortion, followed by irregular bleeding which ceased after a curettage.

In June of 1949, she again became pregnant. Except for a mild anemia, the pregnancy was uneventful. On April 18, 1950, she was admitted to Fairview Hospital about four hours after the onset of labor. The cervix was dilated to 2 cm. Labor progressed slowly. At 2:00 p.m. she was given 75 mg. of demerol and 1/200 gr. of scopalomine. Pains became more regular, and at 2:45 p.m. she was taken to the delivery room. The cervix was now dilated to 3 cm. She was nauseated with her pains, and twice she vomited small amounts of greenish liquid. She was drowsy and slept between pains. At 3:15 p.m. she had an involuntary defecation and urination. At 3:53 p.m. the nurse made the following entries: "Patient turned on side by herself. Became rigid. Head thrown sharply back. Very cyanotic. Does not respond. Patient very cyanotic; respirations gasping. Pulse imperceptible. B. P. 130/60." Various attempts at stimulation and resucitation, including prolonged artificial respiration, were unsuccessful.

An autopsy examination was conducted at 8:00 p.m. of the same day. The lungs were moderately heavy and edematous. The left lung weighed 450 grams and the right weighed 440 grams. The lower lobes were partially atelectatic. The bronchi and the trachea showed no foreign material, and the pulmonary arteries showed no emobli. There was no air in the heart.

Examination of the external surface of the uterus showed no suggestion of trauma, hemorrhage, or other changes. The uterus contained a normal term female infant, which lay with its back anterior and its head down. The membranes were ruptured. About 200 cc. of thick green fluid remained in the uterine cavity, and this was contained in the interspaces between the legs and the arms and in the space around the neck. The fetal head was in the lower uterine segment. The membranes had separated along the lower part of the uterine wall and the muscle of the lower uterine segment was bare for distances varying from 2 to 4 inches. On the exposed posterior wall of the uterus, a small depression was observed, which, when explored with the tip of a forceps, proved to be a sizeable channel. A rubber catheter, such as is used for male catheterization, easily passed through the opening into the interior of the uterine wall and appeared in the large veins in the right broad ligament. Blood recovered from the right common iliac vein and from the lower vena cava, when spread out on the white porcelain tabletop, showed numerous flakes of green mucoid material. One of the larger pieces was about 1 mm. in diameter and 5 or 6 mm. in length.

Approximation of the fetus into its original position within the uterus indicated that the opening into the uterine vein was in about the position of the space formed by the fetal neck and the small parts.

Microscopic study showed approximately the same picture in all the lobes of the lungs. In every section there were many small arterioles and capillaries containing foreign material made up of squamous epithelial debris, amorphous material, mucus and leukocytes. A few foci of leukocytes were present in the lung parenchyma which had the appearance of beginning exudation.

One receives two impressions from this microscopic study of the lungs. The early exudative reaction suggests that the embolism of amniotic sediment was not a terminal explosive event but had been going on for many minutes or even hours. Perhaps the patient's nausea, vomiting, involuntary bowel movement and involuntary urination indicated the beginning of the embolism. The second impression is that the degree of embolism produced only moderate vascular occlusion and that death was due to causes other than mechanical obstruction. It is very likely that "shock" similar to that caused by foreign material in a blood transfusion may have been the final cause of death.

In the past twelve years, there have been seven other maternal deaths at Fairview Hospital; cardiac decompensation associated with old rheumatic valve lesions (two); heart failure associated with lues (one); fulminating eclampsia (one); abdominal complications following cesarean section (one); and pulmonary embolism (two). Unfortunately neither of these two cases of maternal death attributed to pulmonary embolism came to autopsy, and the cause of the deaths could not be confirmed.

The first of these so-called embolic deaths occurred in 1940. The patient, a primipara, was admitted on June 18, 1940, in the care of Dr. M. P. Baken. She was delivered of a normal female infant after an eight-hour labor. The baby was born at 11:05 a.m., and the placenta was expressed at 11:09 a.m. At 12:00 p.m.

the blood pressure was 100/68. At 2:00 p.m., the nurse recorded that the patient was cold and clammy. There was no bleeding and the blood pressure was 100/68. At 3:00 p.m. the pulse was 82 and was weak. The patient was cold and perspiring, and the blood pressure was not obtainable from this time on. The hemoglobin was 74 per cent (Sahli) and the red blood cell count was 3.7 million. At 5:00 p.m., the patient was nauseated, and at 7:00 p.m. she vomited. At 8:00 p.m. she complained of shortness of breath and pain in the abdomen. At 8:15 marked dyspnea set in, and respirations became difficult and labored. The patient died at 8:50 p.m. Death occurred eight hours and fifty-five minutes after delivery and six hours and fifty minutes after the initial observation that the patient was "cold and clammy."

The second of these deaths attributed to pulmonary embolism occurred on April 2, 1948. This patient, a twenty-three-year-old primipari, was admitted to Fairview Hospital in the care of Dr. W. D. Brown on April 1, 1948, in normal labor at term. The child was born at 10:17 p.m., and the placenta was delivered at 10:20 p.m. The patient was moved to her room at 11:05 p.m. The blood pressure was 130/72. At 12:00 midnight, she was examined by the nurse, who charted that the fundus was firm and there was moderate bleeding. At 12:10 a.m. the nurse recorded the following: "Patient screaming for water. Apparently having air-hunger, coughing frothy blood from mouth and nose. Patient extremely apprehensive. Unable to hear blood pressure. Pulse 130, weak and irregular." Cyanosis developed very quickly, and the patient expired at 12:25 a.m., fifteen minutes after the onset of the seizure.

It is impossible, since autopsy examinations were refused, to be certain of the exact cause of death in these two instances, but the probability is very great that it was amniotic fluid embolism. If this explanation is accepted, amniotic fluid embolism accounted for three of the eight maternal deaths in this hospital.

Amniotic fluid embolism was first brought to the attention of the medical profession in 1941 by Steiner and Lushbaugh,[18] who reported eight cases. In the following year they reported two more cases.[9] It was their impression that embolism by amniotic fluid, instead of being a rarity, was the most common cause of death during labor or within the first few hours thereafter.

Since Steiner and Lushbaugh's initial study, numerous other reports have been published. Hemmings[5] in 1947 presented the eleventh published case, and in conjunction with this case study he reviewed 254 maternal delivery deaths and found that the attending physicians had attributed the deaths to pulmonary embolism in thirty-seven (14.5 per cent). These clinical diagnoses were not confirmed by autopsy studies. Hemmings also called attention to a survey of delivery deaths in New York City, in which 7.4 per cent were attributed to embolism, and to another in Philadelphia, in which 11.2 per cent were thought to be due to embolism. Gross and Benz[4] in 1947 reported three cases, all occurring in their practice within one year.

In spite of such indications of fairly common incidence, cases of amniotic fluid embolism actually confirmed by autopsy studies are rare. As late as 1948 Watkins[19] found only eleven recorded cases confirmed by autopsy, and he added one more. Mallory and his group[10] in 1950 reported three cases, which were the first confirmed by autopsy in the State of Massachusetts.

Restudy of all the autopsy material from cases of maternal death at both Boston City Hospital and the Boston Lying-In Hospital failed to show any cases of amniotic fluid embolism. May and Winter[12] restudied autopsy material from eighty-one post-partum deaths and could not find a single instance of amniotic fluid embolism. Steiner and Lushbaugh[9,18] reported their ten cases in 1941 and 1942, but it was not until seven years later (1949) that they, together with Frank, reported another case.[17] Up to the present time, there appears to be about thirty-two cases recorded. Hemmings'[5] study of embolic maternal deaths reveals an amazing low percentage of autopsy examinations. This difficulty in obtaining consent for autopsies may be partially due to the confusion and grief attending the tragic and unexpected death. Actually, because of this exclusion of some of the cases of sudden unexpected death, the reported autopsy series may not be a good representation of the entire group of maternal labor deaths.

It was brought out by Gross and Benz[4] that blood should be aspirated from the right side of the heart in all cases of maternal delivery death. Such an aspiration is permissible since it can hardly be construed as a mutilation of the body. The procedure may be of great value, not only if autopsy permission is refused, but also if embalming is carried out prior to an autopsy study. By centrifuging the aspirated blood, the various elements are layered out. In case of amniotic fluid embolism, the floating elements can be recovered from the surface of the serum and the remaining amniotic debris from the top of the leukocytic "cream" immediately under the serum layer. In our case, blood from the vena cava was spread on the porcelain top of the autopsy

table, and numerous flakes and strands of green mucoid material could easily be seen. Shotten and Taylor[16] reported the first case where particles of vernix could be seen grossly in the heart's blood.

Even though the total number of cases is small, the general pattern and sequence of symptoms is quite uniform. The patient most often is a multipara who is in active labor and is having hard uterine contractions. The clinical picture is that of shock and respiratory distress occurring either during labor or shortly thereafter. Symptoms develop abruptly, or at least very quickly. Often there is preliminary nausea and vomiting. The patients show an abrupt and severe drop in blood pressure. They are cold, clammy, and have a weak, fast pulse. The respirations are rapid and often gasping. There may be air hunger, cyanosis, and pulmonary edema. Uterine bleeding occasionally is present. This may be due to relaxation of the uterus secondary to the shock and the collapse. However, bleeding may occur elsewhere—for example, from the nose, from the lung, into the abdomen or mesentery. Weiner and Reid[20] noted that thirteen of twenty-two reported cases had some hemorrhagic manifestation. They believe that amniotic fluid in the circulating blood interferes with the clotting mechanism.

More than a third of the mothers died in the first hour after symptoms developed, and about three-fourths died within five hours. The remainder lived longer, and one lived eleven and one-half hours. One patient died from associated conditions on the seventh day. Steiner and Lushbaugh[9,18] believe that not all cases are fatal. In one of their cases death was due to other causes and the presence of amniotic sediment in the lungs was only a secondary finding. This observation, together with their experimental work, indicates that survival can occur.

Study of the reported cases indicates that there is no specific etiology. It is obvious that congenital disturbances in the structure or position of blood vessels cannot be a factor, because the majority of patients have had previous pregnancies without any complications. Many contributory factors have been suggested. Steiner and Lushbaugh[9,18] suggest that intact membranes or closure of the uterine outlet by the fetal head, together with hard uterine contractions, may force amniotic fluid into the placental veins. Leary and Hertig[8] demonstrated squamous cells from the amniotic fluid within the placenta and its membrane, and suggested that such extravasation is not uncommon in labor. Landing[7] found squamous cells present in the uterine vessels in from one-third to one-fourth of the uteri removed as operative or autopsy specimens in cases of placenta acreta, ruptured uterus, cesarean section, retention of placenta and premature separation of the placenta. In three of his cases, squamous cells from the amniotic fluid were found also in the lungs. These studies indicate that the entry of amniotic fluid into uterine vessels may not be uncommon and that subclinical or mild forms of amniotic fluid embolism might occur.

In about one-half of the reported cases, some tear or surgical incision into the uterus, cervix or placenta was present. Our case is unique in that a very large communication between the uterine cavity and the maternal circulation was demonstrated.

The sequence of events during amniotic fluid embolism has been postulated by Shenken, Slaughler, and DeMay[14] as follows: The outlet to the uterus is closed by the fetal head. The amniotic fluid, containing considerable debris, is trapped above it. A tear exists in the veins of the placenta or the uterus, and the uterine contractions force the trapped fluid into these open vessels. Most cases occur during labor, which indicates that active uterine contractions are a factor in the process. However, in about one-fourth of the reported cases, symptoms developed after delivery. Presumably in such cases, the open vessels exert a suction effect upon the remaining uterine contents and must actually aspirate the material from the postpartem uterine cavity.

It is believed by the various authors that death in these cases of amniotic fluid embolism is not due to purely mechanical obstruction of the pulmonary circulation. The manner of death is similar to that resulting from the intravenous injection of improper fluids or the transfusion of contaminated blood. The anaphylactoid reaction probably is associated with spasm of the pulmonary vessels. Death may be hastened by postpartem hemorrhage due to uterine atony.

The diagnosis of maternal embolism by amniotic fluid can be verified only by the demonstration of amniotic fluid sediment in the heart or lungs either by autopsy or cardiac puncture. However, there must be non-fatal cases, and these, of course, cannot be confirmed in this way. Seltzer and Shuman[15] reported a case in 1947 in which embolism apparently occurred eighteen

minutes after delivery. A state of collapse lasted for thirty-six hours and was followed by recovery. Unquestionably the diagnosis of non-fatal amniotic fluid embolism is justified, but the diagnosis should not become a shelf upon which to place all cases of obscure obstetrical shock or unexplained death.

In some of the fatal cases death did not occur for several hours and in one not until after eleven and one-half hours. There is time, therefore, to carry out various therapeutic procedures. Active therapy may not be a useless gesture, since it is conceivable that if the patient could be carried over the initial period of shock, she might survive.

Active treatment consists of combating the collapse and preventing or treating pulmonary edema. On the basis of experimental studies, Steiner and Lushbaugh,[9,17,18] suggested that papaverine may be of help in abolishing the reflex vascular spasm in the pulmonary vessels, thereby helping to decrease the obstruction to the pulmonary circulation and to prevent pulmonary edema. Atropine may help to abolish the cardiac depressor reflexes from the lung. Adrenalin probably is contraindicated because of the tendency to increase the spastic obstruction to the pulmonary blood flow. An ordinary blood transfusion may increase the danger of pulmonary edema. However, an intra-arterial transfusion should be of tremendous benefit in combating peripheral vascular collapse. Oxygen should be given if pulmonary edema has already developed.

## Conclusions

Embolism by amniotic fluid is a rare and unavoidable accident of labor. It can occur either during labor or immediately thereafter. Presumably, the amniotic fluid can be forced into the open veins by uterine contraction or can be aspirated by the vessels after the uterus is empty. Death is due to the toxicity of the material rather than to mechanical occlusion of the pulmonary vessels. There is some evidence that individuals may survive, and active treatment of shock may increase this survival rate.

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# EXSTROPHY OF THE URINARY BLADDER

## Discussion of Anatomical and Surgical Principles Applicable to Its Repair, With Preliminary Report of a Case

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THOUGH sporadic attempts have been made to relieve this condition by plastic procedures, the results have not been consistently satisfactory, and the recent feeling widely expressed and recorded has been that ureterointestinal implantation and cystectomy is the only practical treatment.[6,7,8,10,12] The dangers and disadvantages of that treatment (principally pyelonephritis and hydronephrosis) have been so widely discussed as to need no further mention here.[1] The methods of turning the bladder or trigone into the rectum with preservation of the ureterovesical sphincters offer some protection to the kidneys, and the method of Boyce and Vest[1] reported to the American Urological Association in 1951 deserves commendation.

But all those methods are admittedly compromises. Review of the literature finds scattered attempts at plastic repair of the urinary tract without opening the intestinal tract. Most of these attempts have left the patient incontinent, and so have failed. An extremely few, one or two in Europe[9,11,13] and the well-known case of Hugh Young in this country,[15,16] have achieved repair with control of urine, but time has not proved that these results could be repeated by the authors or by others.

The operation reported by J. Edward Burns[2] in 1924 seemed to me to hold out the best promise, but in a later discussion elsewhere Cunningham[3] reported that Burn's patient was still incontinent, even though his bladder was closed, and that therefore the treatment had failed. Cunningham's feeling that "the overcoming of incontinence is the main object and can be accomplished only by diverting the urine to the bowel" seems to be still the prevailing opinion today.

Still we feel that Burns made a very important and unappreciated contribution in insisting that the bladder be placed in the bottom of the pelvis with obliteration of the retrovesical peritoneal pouch so that any increase in intra-abdominal pressure would push the bladder down and not forward against the anterior abdominal wall.

In the early weeks of embryonic life, the retroperitoneal pouch extends down to the apex of the prostate. The deeper part of the pouch is obliterated during fetal life, the opposing peritoneal surfaces coming together as the layers of Denonvillier's fascia.[14] The method of Burns accomplished the same result.

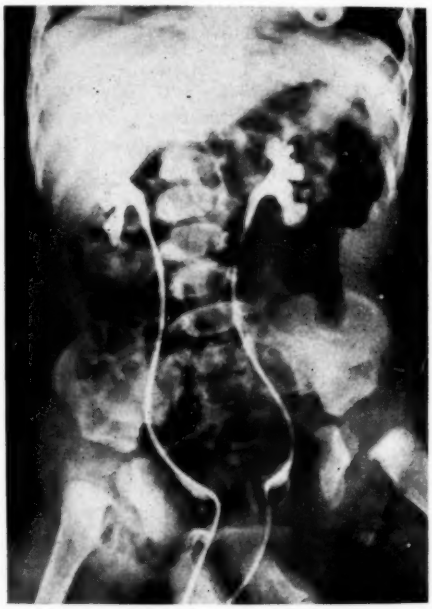

Fig. 1. Preliminary pyeloureterogram at age four months.

It seemed to us that perhaps Burns failed to eliminate incontinence because he used an open perineal operation for repositioning of the bladder and so possibly injured the nerve supply; it is recognized that operations of the prostate through the pelvic floor carry some danger of urinary incontinence. The simplified method for repositioning the bladder should avoid that danger and thus help in insuring a good functional result. With the bladder well down in the pelvis, the obtaining of urinary control should be possible in spite of

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the prevailing skepticism. Years after the report by Burns F. K. Garvey[5] showed a beautiful movie depicting the cure of epispadias with incontinence in the female, and in October, 1949, Dees[4] read the excellent paper on the cure of epispadias with incontinence in the male. Both authors reported good urinary control and voiding. It seems to us that placing the exstrophic bladder in its normal position in the bottom of the pelvis should reduce the problem to the same problem that Dees and Garvey had for the cure of epispadias with incontinence.

Construction of the urethra by the Dees method after repositioning of the bladder results in a normal S-curve of the urethra, as shown in the lateral urethrocystogram. Probably that also is an important factor in accomplishment of urinary control.

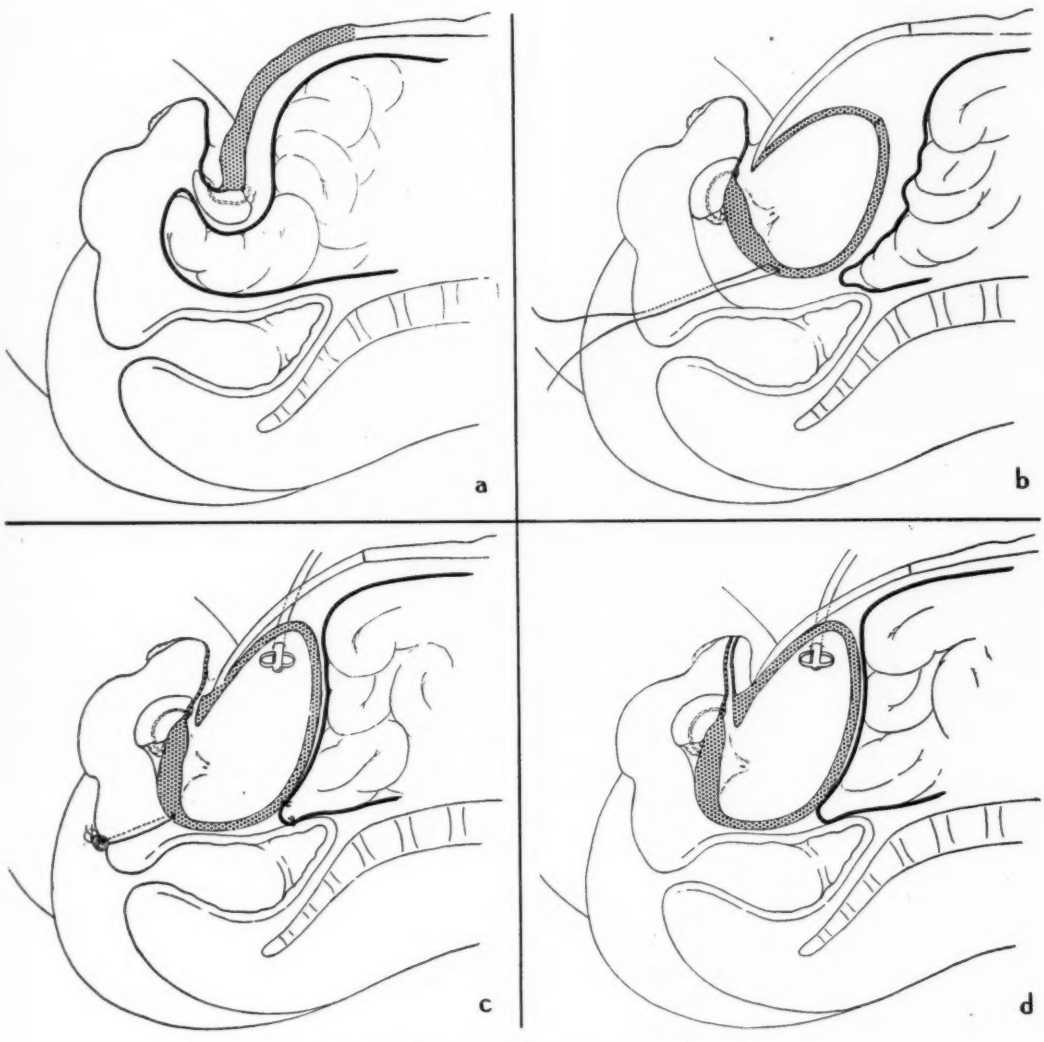


Fig. 2. Median sagittal diagrams to show stages in the operative treatment:

(a.) The condition before operation.
(b.) The bladder freed, the peritoneum freed from bladder and rectum and pushed up, and the first mattress suture passed out through perineum.
(c.) The first operation completed; the bladder fastened down in place, the peritoneum displaced upward, the bladder and posterior urethra closed.
(d.) The second operation completed; the epispadias repaired.

One other problem remains: the age at which such operations should be done. There seems to be a widespread feeling that the operation should wait until the age of four to seven years though

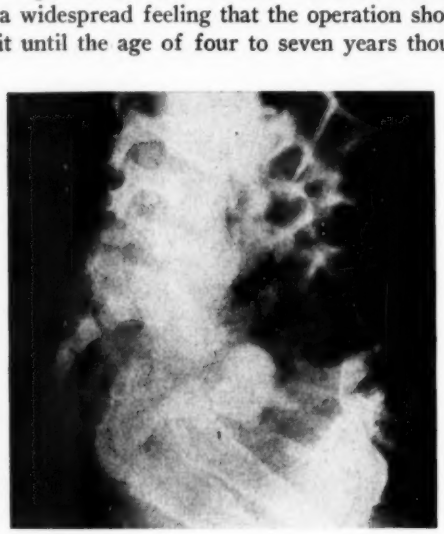

Fig. 3. Lateral cystograms showing the bladder in normal position in the bony pelvis.

in the last few years Higgins,[8] Meredith Campbell, and some others have recommended ureterosigmoid anastomosis before the age of one year. We feel that the first plastic operation should be done by the age of six months in order to avoid the structural changes due to mucosal exposure and infection, and the second operation may safely be done before the age of eighteen months, even though voluntary urinary control is not certain in normal children at that age.

## Case Report

This boy was born October 15, 1950, apparently normal excepting a typical exstrophy of the bladder with wide anterior defect of the abdominal wall and bony pelvis, bilateral subluxation of the hips and bilateral inguinal hernia. It was advised that surgical treatment be postponed for five or six months to avoid the general surgical risks of the newborn.

On April 16, 1951, retrograde ureteropyelograms were made (Fig. 1) which demonstrated normal upper urinary tracts with the exception of slight dilatation of the lower parts of both ureters. The thick bladder wall lay open on the lower abdominal wall. Clear urine came forth from both ureters normally. The open bladder extended downward from the area of the umbilicus to an open depression at the site of the bladder outlet, which was continuous with the wide open urethra (Fig. 2a); the corpora cavernosa of the penis were behind the shallow groove of the open urethra which extended beyond to the end of the glans penis. Testes were in the scrotum.

On April 17, 1951, at the age of six months, the first operation was performed. An incision was made around the junction of the bladder wall with the abdominal wall. The dome of the bladder was freed from the peritoneum

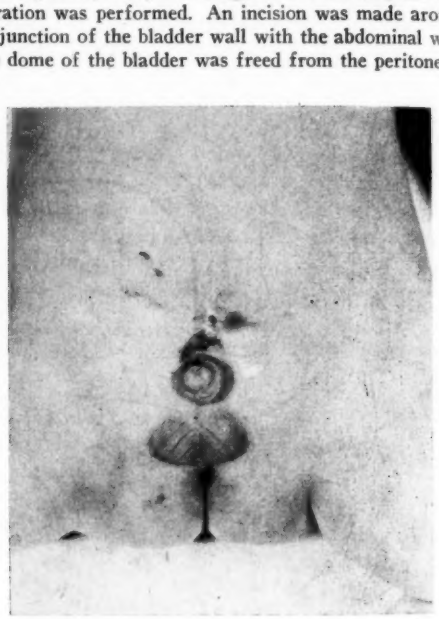

Fig. 4. Photograph of the boy at age nineteen months, three months after the second operation.

part way down laterally and posteriorly. The peritoneum was then opened and the pelvis explored and the hernias closed from inside. On exploration the pelvic peritoneal pouch extended clear to the pelvic floor beyond the apex of the prostate (the embryonic state); the rectum and sigmoid were normal. The peritoneum was then further freed from the bladder clear to the bottom of the pouch and then upward from the rectum. A silk suture was then placed in the bladder muscle at the midline posteriorly just above the trigone, and its long ends passed out through the perineum on needles well to each side, a finger being in the rectum to prevent damage to that organ (Fig. 2b). Another silk suture caught the posterior bladder wall to each side of the midline suture, avoiding the ureters, and its ends were similarly passed out through the perineum. The ends of those two silk sutures were later tied over short pieces of rubber tubing on the skin of the perineum. The freed peritoneum was then attached to the anterior wall of the rectum and the posterior wall of the bladder high up to obliterate the deep peritoneal pouch previously present. The thoroughly freed bladder was then closed in the midline anteriorly with drainage by wing-tipped catheter passed out through a stab wound in the right anterior bladder wall and right rectus muscle. The bladder outlet and deep urethra were narrowed by removing a triangular piece of mucosa at each side before closing over a No. 10F soft rubber catheter as described by Dees, the catheter being then removed. The anterior abdominal wall was then closed over the bladder and deep urethra by turning a triangular flap of each rectus sheath over

the midline and downward with considerable overlapping and without tension using silk sutures. The skin was closed over it. Convalescence was smooth and result thus far satisfactory (Fig. 2c).

On July 11, 1951, the anterior epispadias was repaired by the method of Dees over a No. 10F soft rubber catheter, but the catheter unfortunately was left in place and most of that repair broke down. On February 7, 1952, at the age of sixteen months, examination with an infant panendoscope showed a good bladder of about 50 cc. capacity with a satisfactorily closing outlet. Repair of the distal urethra was again carried out, the urethra being closed with No. 0000 chromic catgut sutures, and the overlying tissues with fine wire sutures tied over a small vitheline tube at each side. The urethral catheter was then removed, leaving only a nylon thread extending through the urethra and bladder and out alongside a newly placed suprapubic drain (Figs. 2d, and 3).

The repair of bladder and urethra have healed well excepting a pinpoint fistula at the base of the penis. Voiding is in considerable amounts from the normal urethral meatus on the glans with a good stream, though there is a little leakage under stress only from the pinpoint fistula (Fig. 4). The urine is clear. While, of course, no final statement as to urinary control can be made at this time, at present the condition seems to be what normally could be expected from a child of this age.

## Conclusions

The widespread defeatist attitude regarding plastic operations for the relief of exstrophy of the urinary bladder is not justified.

The rosy picture of the life of the patient after ureterosigmoid implantation is also unjustified and it is not even certain that such a patient has a better outlook than one who has no surgical treatment at all.

We believe that the presently described two-stage operation for (1) repositioning and closure of the bladder, anterior abdominal wall, and posterior urethra, and for (2) closure of the distal urethra can be confidently expected to result in normally functioning bladder and urethra with good urinary control.

Sympathetic co-operation between the urologic and pediatric surgeons, the pediatrician, the anesthetist, and the parents is of great value in ensuring a good result by permitting operation at an early age.

## Acknowledgment

The excellent work of the anesthetist, Stanley P. Wesolokski, M.D., and of the artist, Jean Hirsch Fish, is gratefully acknowledged.

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## BRITISH DOCTORS GET PAY HIKE

The 20,000 doctors under Britain's socialized medicine setup finally received their pay increase, which will cost taxpayers nearly $100,000,000 between now and next March. The raise, retroactive to the start of the socialized medical service in 1948, represents an average payment to each doctor of nearly $5,000.

The raise came after the doctors threatened to leave the scheme high and dry last year.

Doctors at present earn $1.70 a year for every patient on their books, and they can have 4,000 patients. The average, however, is 2,300. The increase will mean about $1,500 more yearly.—*Secretary's Letter A.M.A.*, July 14, 1952.

# RECENT ADVANCES IN THE DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE CERVIX

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I HAVE chosen as my subject one that offers a great challenge to us because it concerns a lethal disease and a relatively common one. Next to carcinoma of the breast, cervical cancer is the most common malignant lesion in women. Today approximately one out of four women who are treated for this disease die as a result of it. And yet, I will point out to you that there is great hope of bettering our salvage from this serious neoplasm. Fifteen years ago cervical cancer would have been about as dead a subject as one could select. The diagnosis of cervical cancer was made from a gross and usually advanced lesion; the diagnosis was confirmed by biopsy and the treatment was irradiation. Today, it is one of the most controversial subjects in gynecology. The renewed interest has been due chiefly to progress in three directions:

1. The discovery and proven practical use of cytology, as demonstrated by Papanicolaou and Trout.
2. The recognition of carcinoma *in situ* and a better understanding of its relation to invasive cervical cancer.
3. A re-valuation of the surgical technique in the treatment of cervical cancer.

Before we discuss our newer knowledge of the disease, let me emphasize a few of the things that we have known about the symptomatology and diagnosis for many years—things that are all too frequently forgotten or disregarded by many practitioners. This is regrettable because practitioners are our first line of defense against this malignancy, and failure to diagnose and treat it properly at the first opportunity often means that the only opportunity of cure has been lost.

Cervical cancer is not primarily a disease of old age. The average age is forty-eight years, but many cases occur in the thirties and some in the twenties.

Cervical cancer is not limited to parous women. About 10 per cent of our cases occur in nulliparous women, and that figure is probably pretty close to the percentage of nulliparous women in that age group.

Cervicitis probably predisposes to cervical cancer. The absolute proof of this statement is difficult, but there is strong evidence to support it. Several years ago Pemberton and Smith at the Woman's Free Hospital in Boston found an almost complete lack of cancer in a large group of women who had been properly treated for cervicitis. More recently Gagñon, who has had a wide gynecological experience among the nuns of Quebec, city and province, found an almost complete lack of cervical cancer among this group of women, in whom cervicitis occurs at a minimum. Cancer of the corpus uteri, on the other hand, was found to be as common among nuns as in the general population.

Although cervical cancer may proceed to a relatively advanced stage before giving rise to symptoms, in the majority of the cases abnormal uterine bleeding takes place when the disease is curable. If the lay public could be informed of this single fact and the practitioners could be made to carry out the necessary simple diagnostic procedures, such as the inspection and biopsying of all cervices of women with intermenstrual or postmenopausal bleeding, there would be a tremendous increase in our cure rate of this disease.

In the State of Maryland we are spending some of our cancer society money in an attempt to find out the reason for delay in diagnosis after the appearance of abnormal uterine bleeding. There has been functioning for the past six months a committee of the state medical society to determine where and why there is so frequently a delay. We have a secretary-social-worker who interviews patients with pelvic cancer at the participating hospitals in an attempt to learn from the patient the date of the appearance of the first symptom, the date of her first visit to her family physician, the type of examination done, the type of treatment instituted and the time of her reference to a qualified clinic or gynecologist. With the proper social worker this interview can be done without arousing the slightest suspicion on the part of the patient. Once a month the com-

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mittee selects a certain number of these cases in which there has been delay and discusses them at an open meeting to which every doctor who has had any connection with the case is invited. The cases are anonymous and the doctors concerned are anonymous to all except the chairman. In the case summaries given out to the audience the doctors are designated as Dr. A, B, C, et cetera. Discussion is free and frank. If the attending doctors wish to declare themselves, they are at liberty to do so, and not infrequently they bring in extenuating facts which may explain the delay in treatment. When a practitioner leaves the meeting he should know without any doubt that he has done wrong if he has given a woman estrogens for bleeding in the menopausal age without doing a complete pelvic examination. We consider that there has been "delay" when there has been the loss of over one month of time between the appearance of the first symptom and the institution of proper therapy. We have found patient delay about three times as frequently as physician delay, but it is most revealing to find out how often the chance of cure is missed by failure of the physician first consulted to make a proper examination. The meetings are conducted not in a critical way but with the hope of educating those members of the profession who are not as cancer-minded as they should be.

Papanicolaou smears have now been used widely enough so that the practice may be fairly evaluated. Since the establishment of cancer detection centers in Maryland we have routinely biopsied and taken smears of all women coming to the center. We are not convinced that this double procedure should be carried out routinely, but we have done it as a study to evaluate both the smear and biopsy techniques and to compare them. In a series of 2,321 cases we have found the following:

| | | |
|---|---|---|
| Total number of smears and biopsies | 2,321 | |
| Smear and biopsy benign | 1,939 | |
| Smear and biopsy—carcinoma | 79 | |
| False positive smears | 27 | 1.1 % |
| False negative smears | 17 | 0.73% |
| Doubtful smears | 179 | 7.6 % |
| Unsatisfactory smears | 78 | 3.3 % |
| Positive smear correct—negative biopsy incorrect | 2 | |

An analysis of the doubtful smears follows:

| | | |
|---|---|---|
| Total number of doubtful smears | 179 | |
| Biopsy benign | 135 | 74.9 % |
| Basal cell hyperactivity | 19 | 10.6 % |
| Biopsy carcinoma | 25 | 13.9 % |

If one checks the smears of a series of proved carcinoma cases, the results are as follows:

| | | |
|---|---|---|
| Total number proved carcinomas | 129 | 100 % |
| Biopsy positive | 127 | 98.5 % |
| Smear positive | 81 | 62.8 % |
| Smear doubtful | 25 | 19.3 % |
| Smear negative | 17 | 13.7 % |
| Smear unsatisfactory | 6 | 4.7 % |
| Biopsy negative | 2 | 1.5 % |

From the above analyses we have concluded that the smear technique is of great value as a screening process of the "normal" female population. The percentage of errors will be very small, but the percentage of errors by biopsy will also be very small. We believe that the two procedures should not be considered as competitive but as complementary. If both procedures are carried out on *suspicious* cases, there will be very little chance of error. However, when dealing with advanced cervical cancer the sloughing necrotic cellular debris makes the chance of error by smear fairly high. In such cases there is little point in making a smear. The gross lesion can usually be readily seen and biopsied and an unequivocal diagnosis promptly made. Therapy should never be carried out on the report of a positive smear, unconfirmed by biopsy. When biopsy is doubtful, we have found sharp conization of the cervix with extensive microscopic study of all of the tissue to be most useful. We have not found cytology to be very helpful as a means of following response to therapy or of determining whether further therapy is indicated. There are too many abnormal cells found in smears after irradiation to make cytologic study valuable. In fact, we believe it can be very misleading. It is perhaps unnecessary to say today that cytologic diagnoses should only be made by trained cytologist. Even a well-trained pathologist may not be a competent cytologist. Finally, it should be emphasized that cytology is time-consuming and expensive. Most of the cytologic laboratories operating today are endowed and are not paying their own way.

Within the past decade the question of carcinoma *in situ* has become an important one in the minds of most gynecologists. Opinion is not crystallized on this subject among gynecologists or among general pathologists. There are three vital questions that should be answered:

1. What is carcinoma *in situ?*
2. What is its relation to invasive cervical cancer?
3. How should it be treated?

I shall attempt to answer the question—what is carcinoma *in situ*?—first. Probably the first case of carcinoma *in situ* ever to appear in the literature was described by Rubin in 1910. He did not call it by its present name but simply described and pictured two early cases of cervical cancer. Two years later Schottländer and Kermauner described the same microscopic picture in the surface epithelium around the periphery of advanced cervical cancer. It was Walter Schiller who first conceived the idea that perhaps invasive cervical cancer in its early stage existed for a prolonged time as intraepithelial, only to become invasive months or years later. By definition, then, carcinoma *in situ* is a condition of the surface cervical epithelium in which the individual cells have every characteristic of invasive cancer cells, but they remain on the surface or displace the columnar epithelium of the cervical glands. By common consent most students of the disease have agreed to include as carcinoma *in situ* the cases in which the glands have been invaded. It should be emphasized that carcinoma *in situ* is a histopathological diagnosis which applies only to the microscopic picture within the microscopic field. Actually the cervix from which that bit of tissue has been obtained may harbor carcinoma only on the surface epithelium. It may also harbor glandular "invasion" or it may harbor invasive cancer. The invasive cancer may even be extensive as it was in Schottländer and Kermauner's original cases. So let us remember that when we use the term "carcinoma *in situ*," we are not describing the entire neoplasm.

Now let us consider the second question: the relation of carcinoma *in situ* to invasive cancer We know from Schottländer and Kermauner's description that it *may* occur on the periphery of invasive cancer, but is that only a coincidence? Does carcinoma *in situ* proceed to invasive cancer and, if so, how frequently? Is invasive cervical carcinoma invariably preceded by carcinoma *in situ*. I should like to throw some light on these questions from our own experience. Our first experiment consisted in biopsying the cervix of every patient on the ward service on whom we planned to perform a hysterectomy for myomata, recurrent functional bleeding, et cetera. In those cases in which carcinoma *in situ* was found on biopsy the cervix which was removed by total hysterectomy was cut into several blocks and semi-serial sectioning was done of each block. A careful study was made of each section. In approximately three-fourths of the cases we found either gland "invasion" or true invasion. The actual percentage of true invasion is difficult to ascertain because there are too many cases in which the differentiation between glandular invasion and true invasion is equivocal. That is about all the evidence that we are able to produce by purely histologic study.

There is something to be learned by following these cases clinically. We had seen a few cases in which clinical invasive carcinoma had developed where a previous biopsy showed intra-epithelial carcinoma. Other similar cases began to appear in the literature, and this was *suggestive* that in at least some instances pre-invasive cancer precedes the invasive growth. This could be a coincidence if it occurs only occasionally, so it is highly important to know how frequently invasive cancer is preceded by the pre-invasive type. From 1941 to 1951, inclusive, we treated 723 cases of cervical cancer. We found on going through the histories of these women that thirteen of them had had their cervices biopsied in our clinic from one to seventeen years before. We still had the slides and blocks of tissue available for study. Upon making a study of the early slides or of slides obtained by cutting more sections of the blocks we found carcinoma *in situ* to be present in eleven of the thirteen cases. In one case there was no epithelium present in the block so it must be excluded. That reduced the cases for complete study to twelve. In the twelfth case a diagnosis of intra-epithelial carcinoma could not be made, but there was much evidence of hyperactivity of the basal epithelium. It appears to us that the pre-existing presence of carcinoma *in situ* in eleven out of twelve cases available for study is very significant. The shortest time interval between the initial biopsy and the discovery of the clinical cancer was one year and longest time seventeen years. It appears, then, that in the vast majority of cases in which study was possible pre-invasive cancer existed before the development of clinical invasive cancer. But that is not to say that this invariably is the case—nor can it be said that intra-epithelial carcinoma invariably becomes invasive cancer. I think in our present state of knowledge we would have to say that the latter is not true. Knowing, as we do, that carcinoma *in situ* may remain non-invasive for many years, it is quite certain that many women die of other diseases before the carcinoma becomes invasive. In our present state of knowl-

edge it would appear that clinical cervical cancer, as we have been accustomed to think of it, is only a short span of the complete life of the carcinoma. This is borne out by the fact that the average age of the women in our series with cervical cancer is thirty-six years and the average age of clinically invasive cervical cancer is forty-eight years.

Our treatment of carcinoma *in situ* has been removal of the entire uterus with a moderate amount of parametrial tissue and a reasonable vaginal cuff. We believe that he vaginal cuff is the most important deviation from the ordinary total hysterectomy technique because often the cervical lesion extends to the very edge of the cervix and in a few instances to the vaginal cuff. In young women we have on several occasions saved one or both ovaries. We have now operated on over 150 such cases, and all of the women are well. Slightly over fifty of them have been well for more than five years after their operation. During this time we have treated eight cases of intra-epithelial carcinoma with irradiation. Among them there was one death, and, strangely enough, it occurred within six months after treatment. Autopsy showed metastatic cancer. Since our original study required a histological examination of the removed cervix, our original treatment was by surgery. The results have been so good that we have hesitated to change to irradiation although there is little doubt that a high percentage would be salvaged by irradiation. Another advantage offered by surgery is the preservation of ovarian tissue in the younger patients. Since many of the patients are in the third decade, the desirability of saving ovarian function is obvious.

There is no doubt from our results that we are treating these patients adequately. The question may justly arise as to whether we are overtreating them. Fortunately, all of the students of this disease have not approached the problem the same way. Paul Young, for example, has tried to evaluate his cases before treatment to a fine degree as to glandular and true invasion by extensive biopsying. Those in which the disease is strictly limited to the surface epithelium he has treated by catuerization, conization or amputation. Of forty-one cases treated thus conservatively, fourteen subsequently required further treatment for cervical cancer. Young has done an important experiment. How shall we interpret the result? Personally, I believe that such treatment is not justifiable when fourteen of the patients require further treatment for a lethal disease. It is true that some children have been born to women in Young's series after the diagnosis of carcinoma *in situ* was made, but one cannot help but wonder whether this calculated risk is justifiable. In my opinion it would be justified only under most unusual circumstances and when the patient is under very close observation by an expert. The weak point in attempting to evaluate accurately the extent of the disease preoperatively lies in the fact that one never knows the extent of the disease until the entire uterus has been removed and carefully studied microscopically. Our pathological material has shown this repeatedly.

I hope that what I have said about the surgical treatment of carcinoma of the cervix *in situ* will not be construed as applicable to invasive cervical cancer. I firmly believe that the treatment of invasive cervical cancer is irradiation. There are a few exceptions to this general rule, of which I will speak later. In order to form an opinion regarding therapy for this disease, one should look at the question historically. At about the turn of the century Cullen reported in his classical volume on *Cancer of the Uterus* that 26 per cent of the cervical cancers that had been operated upon by radical hysterectomy and pelvic lymph node dissection were well five years later. Some years later radium became available, and some of the more advanced cervical cancers were treated with it. In many instances there was surprising improvement and in some instances cure. Then some of the less-advanced cases were treated with irradiation, and the results steadily improved, until in recent years the over-all five-year cure rate with irradiation reached 25 to 30 per cent. Some series have shown better than a 30 per cent five-year cure. These irradiation results are much better than Cullen's operative results because his 26 per cent cure rate was based on only the cases operated upon, whereas the irradiation results were based on all cases seen. For comparison of these irradiation results, let us look at some later operative results. Sir Victor Bonney of London spent his entire active surgical career performing the radical Wertheim type of hysterectomy for cervical cancer. His last report was on the results of 600 operations performed by him. He operated upon 63 per cent of the cervical cancers that he saw and had a five-year cure rate of 41 per cent. If one multiplies 63 by .41, the answer is 25.8, practically the same percentage

of cure attained by irradiation in most clinics. His operative mortality was 14 per cent. In 1950, Charles Read, Bonney's successor, came to this country and spoke on his results with the Wertheim type of radical hysterectomy with lymph gland dissection. He had modified his views considerably from those of his former teacher, Bonney. Operability had been reduced from 63 to 14 per cent, and his five-year cure for Stage I and II combined was 44 per cent. Operative mortality had been reduced to 5.5 per cent, as might be expected with greater selectivity of the cases. The percentage of five-year salvage of Stage I and II from most irradiation clinics exceeds the figure reported by him. For example, Read reports an 80 per cent five-year salvage of Stage I and 61 per cent salvage of Stage II in the Madame Curie Hospital.

The percentage of urinary fistulas resulting from irradiation and surgery is approximately the same, in the neighborhood of 10 per cent. However, these figures are not really comparable. The fistulas resulting from irradiation occur most often in the advanced cases where life expectancy is usually short, whereas the fistulas resulting from surgery occur in the individuals having "operable" lesions. These are the earlier cases which have a good chance of permanent cure. It is one thing to be responsible for a urinary fistula in a woman whose life expectancy is only a year or two and quite another thing to create one in a woman who has a long life expectancy.

Finally, Meigs has carried on a surgical experiment on early cases which were carefully selected as being good operative risks. He has performed over 150 operations, more radical than Wertheim's, without a single death. He has recently reported on eighty-five cases which were operated upon five or more years before. Of his Stage I cases he has a five-year salvage of 80 per cent. This percentage of cures is somewhat better than the usual 70 per cent reported from the better irradiation centers, but the figures are not quite comparable. Meigs' cases were a selected group, and it must be remembered that the patients who are better operative risks also respond better to irradiation. Meigs, then, has shown that in the hands of an expert the results with surgery in Stage I cervical cancer are slightly better than with irradiation. However, these results do not give *carte blanche* to every gynecologist or surgeon to attempt radical pelvic surgery which requires special training and ability. Perhaps one of the greatest sins today in surgery is the attempting on the part of the average pelvic surgeons to do the radical hysterectomy with pelvic lymph gland dissections, only to end up with an incomplete operation. The woman with Stage I cervical cancer has a much better chance of survival when irradiated than when operated upon by the average pelvic surgeon. The more advanced the lesion is, the greater becomes the advantages of irradiation therapy over surgery. In our clinic we perform radical hysterectomy and pelvic lymph node dissection only upon irradiation resistant cases of Stage I and rarely Stage II. The resistance to irradiation therapy can usaully be detected within five or six weeks after irradiation is instituted.

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## GRAY LISTS $137 MILLION SAVINGS, $40 MILLION IN MEDICAL FIELDS

Veterans Administrator Carl R. Gray, Jr., reporting on his four years as head of the organization, lists economies of $137 millions, with approximately $40 millions saved in medical fields. His summary was presented to the House Veterans Affairs Committee. Savings in the medical department (other than in construction and administration) were said to include:

1. Reduction and control of number of physical reexaminations for adjudicatory action—$25,250,000 saved.

2. Standardization of procedure for collection of fees from insurance companies for hospitalization of veterans with non-service connected conditions—$7,200,000, "which would not otherwise have been paid the government by the insurance companies."

3. Inventory and personnel economies in pharmaceuticals—at least $2 million.

4, VA's operation of its own blood bank program—$3 million saved.

5. VA's operation of its own dental laboratories—$2.3 million saved.

The above economies do not represent reductions in overall spending. VA's total budget for fiscal 1948 was $6,922,457,320, with the medical department getting $588,561,819. For fiscal 1952 the total estimated budget was $4,409,265,220, with $703,190,160 for medical activities.—*Capitol Clinic*, July 8, 1952.

# SURGICAL LESIONS OF THE BREAST

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WHEN a physician is confronted with a patient, who recently has discovered a lesion in the breast, his responsibility for an early, correct diagnosis and adequate therapy is tremendous. The end result will be directly related to his knowledge of the underlying pathological process and to his ability to establish a correct diagnosis and institute early adequate therapy. Fortunately, because of an increased awareness on the part of the public, due to widespread education regarding lesions of the breast, patients are presenting themselves at an earlier stage in their disease than they have done in the past. The medical profession has long advocated the need for patients to present themselves early, but only recently have patients been instructed in a systematic thorough method of self-examination of their breasts so that very early lesions might be detected before the pathological process becomes widespread. Much credit is due to the American Cancer Society[17] and others[15] in disseminating to the public this type of valuable information. Better results in the future will be forthcoming.

In the vast majority of cases, lesions of the breasts are accidentally discovered by the patients themselves. Too often when they have been casually discovered they have already assumed rather sizeable proportions and have spread far beyond the confines of the breast. Only occasionally is an unknown lesion of the breast found on routine physical examination. Economically, it is not feasible for a patient to have professional examinations of her breasts often enough for early lesions to be detected. For this reason, periodic self-examinations of the breast as advocated by Haagensen, would seem to offer the best means at our disposal, at this time, in bringing early lesions to our attention. Patients should be taught systematically to palpate their breasts while in the supine position, to note any change in symmetry, any change in the contour of the skin or nipple and to observe if any discharge can be expressed from the nipple. They should be taught that whenever anything that seems to them at all unusual is found, they should present themselves immediately for professional evaluation of their findings.

Physicians should likewise familiarize themselves with a thorough method of examining the breasts of the patient in both the sitting and supine position. Inspection as to changes in the contour of the breast showing the retraction phenomenon of the skin overlying the pathological process is certainly one of the most valuable methods of examination. Indeed, it often gives the clue to tumor before palpation of the tumor can be certain. An attempt to express discharge from the nipple often will give valuable information as to an early lesion of the breast. The need for uniform thorough examinations of the breasts by a physician and correct evaluation of lesions is of extreme importance. In a recent study of a series of breast tumors,[17] it was found that in 27 per cent the patients had been given wrong advice by the first physician whom they consulted.

The breasts are derived from the sweat glands and are composed of fifteen to twenty-five lobes which radiate from the nipples.[8] The lobes are composed of lobules which in turn are made up of acini. The acini are lined by two layers of cells, an inner layer of columnar cells which are secretory in function and an outer layer of flat ovoid cells which are regenerative in function. Separating the acini and lobules are strands of connective tissue which attaches to the skin—the so-called suspensory ligaments of Cooper. These connective tissue septa in disease become fibrosed and contract causing the retraction phenomenon, or dimpling of the skin, which is so often the tell-tale evidence of underlying pathology. Traversing throughout the breast is a network of lymphatics which, according to Adair,[3] drain into nodes in the base of the axilla, then extend into nodes along the subclavian vein to the group lying behind the pectoralis minor muscle. Drainage likewise extends to the nodes in the falciform ligament or extend upwards into the base of the neck or into the mediastium. Knowledge of these pathways is essential in ascertaining the extent of involvement when neoplastic disease is encountered, as well as to what constitutes a radical mastectomy when neoplastic disease is to be erradicated.

Hormones have a profound influence on the

Read at the annual meeting of the Minnesota State Medical Association, Minneapolis, Minnesota, May 28, 1952.

TABLE I. CLASSIFICATION OF BENIGN TUMORS OF THE BREAST

A. *Mammary Dysplasia*
Abnormalities in ovarian function
1. Mastodynia
2. Adenosis
3. Cystic Disease

B. *Benign Neoplasia*
True, benign tumor formation
1. Benign Fibroadenoma
2. Benign Intracystic Papilloma
   a. Papillary invagination of large ducts
   b. Intracystic papillomas
   c. Papillary hyperplasia

C. *Benign Nonindigenous Tumors*
Lipomas, Angiomas, Leiomyomas, Dermoids, Sweat Gland Tumors

breasts. Estrogen causes the rapid growth and changes in the breast at puberty. There are continuous changes in the breast during the menstrual cycle. During the first half of the cycle, estrogen produces a gradual growth of glands. Progestin produces further change in the latter half of the cycle. Once pregnancy is established, progestin causes an increase in the growth of the glands with proliferation of lobule arrangement. Prolactin, a hormone of the anterior pituitary, reacts to produce actual secretion of milk. An understanding of the effect of these hormones will give an insight into the cause of many of the complaints referrable to the breast. Indeed, it is thought that many of the lesions of the breast are expressions of ovarian function.

Unanimity regarding the classifications of benign breast tumors is lacking. Clinicians and pathologists often use different classifications. Geschickter,[10] Copeland,[9] Bloodgood,[6] Cole[8] and others[4] have classified breast tumors. Copeland's classification, based on the work of Geschickter, seems to be a practical one (Table I).

## Mammary Dysplasia

*Mastodynia,* or painful breast, is found most often in women between the ages of twenty and forty years. Married women suffer from this condition three times as frequently as unmarried women. The pain is usually gradual in onset over a period of months and becomes worse just before or during the menstrual period. It often occurs in women with small breasts and it may be present in one or both breasts. The breast tissue in the painful area becomes thicker and more granular than the surrounding breast tissue. At times the disease appears to be a precursor to cystic disease. If biopsied, this nonencapsulated, dense and fibrous tissue may contain small cysts. The normal lobule formation in the breast is dependent on the proper ratio of estrogen and luteal hormones. In mastodynia, it is thought that there is a relative lowering of the function of the corpus luteum or an excessive stimulation by the estrogenic hormones. Progesterone given twice a week for the last two weeks of two consecutive cycles seems to give the most relief to these patients who so often believe their painful breasts are due to more serious lesions.

*Adenosis* (Schimmelbusch's disease) of the breast is characterized by an increase in the fibrous tissue in the parenchyma which is riddled with minute adenomas, papillomas and dilated ducts. These lesions may be found in one or both breasts. The diseased areas are usually thickened and painful, and an edge can be palpated at the periphery of the diseased portion. The age group most commonly affected is from adolescence to forty-five years. Those who develop sexual maturity early with small breasts due to stunting from high estrogenic stimulation often suffer from adenosis of the breast. Also many women over thirty years of age with menstrual complaints often present themselves with symptoms suffered for a year or more. The multiple nodules, which are so often found, are thought to be due to hyperestrinism brought about by a low function of the corpus luteum. If these lesions are observed over a period of years about 2 per cent will become malignant. Estrogenic therapy has proved to be of no value and often makes the condition worse. Progesterone given between two or three menstrual periods has proven to give the most benefit in adenosis of the breast.

*Cystic disease* of the breast is a condition about which much controversy centers. The findings of extensive histological and clinical research by Warren,[30] Campbell,[7] Adair, Bloodgood[6] and others,[1,20] have differed as to whether these lesions should be considered as precancerous lesions. At the present time, it would appear that certain types of cystic disease are more prone to eventuate into neoplastic growths and it may be said that a patient with cystic disease of the breast will develop malignancy more often than the patient with normal breasts. Cystic disease occurs most often near the menopause. Symptoms often come on quickly over a period of a few days to a few weeks. It is frequently seen in childless women in their early forties, first having symptoms of a burning or sticking in their breasts even before a definite lump can be palpated. Multiple cysts

are found in one or both breasts in about 25% of the cases. It is thought estrogenic stimulation results in the formation of the cysts. When these lesions are biopsied, often one or more cysts will be seen or a large single cyst which Bloodgood has described as "blue-domed cysts." Excision will cure the vast majority of these lesions, but a periodic vigilant follow-up should be carried out on all patients with cystic disease of the breast.

*Fibro-adenoma* are composed of fibrous and glandular tissue, their firmness depending on the predominence of either cellular element. They are found most frequently in young women who usually give a history of a painless mass that has been getting gradually larger over a period of a few months. Because of the difficulty in differentiating these benign lesions from early malignancy, excision should be caried out promptly. They are encapsulated and only in a small percentage of cases do they reappear. If they appear at the time of the menopause and go untreated, they often develop into large fibromyxomas or fibrosarcomas.

*Benign intracystic papilloma* occur most frequently in women near or beyond the menopause. They are found as often in nulliparous as in parous women and are due to a papillary invagination of the large ducts. At times the papillary growth may completely fill a cyst cavity. These lesions are usually slow growing and present themselves as a soft mass which is freely moveable and often encapsulated. They are most frequently found in the central zone of the breast and when compressed will present the significant symptom of bleeding from the nipple. Repeated attempts to locate the source of the bleeding is necessary, and when found excision is promptly carried out. Because of the bleeding, they usually command the attention of the physician to ascertain whether or not the bleeding might not be caused by Paget's Disease or other types of malignancy of the breast.[16] Campbell, Geschickter, Adair and others[11,16] found bleeding to occur about as often in malignancy as in benign lesions. If there are multiple sources of bleeding or when limited excision does not remove the entire bleeding process, simple mastectomy is indicated.

*Benign nonindigenous tumors,* such as lipoma, angiomas, leiomyoma, dermoids, should be removed as their presence invariably causes the patient to fear impending malignancy.

*Malignant tumors of the breast.*—Carcinoma comprises the overwhelming majority of neoplasms of the breast. Sarcoma and malignant myxomas are rare. In 6,558 patients with malignancy of the breast seen at the Mayo Clinic between 1910-1940, Harrington[17] found 99.4% to be carcinoma. Carcinoma of the breast is by far the most common malignant lesion in the female (Fig. 1). It is ten times more common in the female than in the male. Carcinoma is found simultaneously in both breasts in about 1% of the cases. About 5% of patients treated for carcinoma of the breast will later develop carcinoma in the remaining breast.

Little is known regarding the etiology of human breast carcinoma. Endocrines, heredity and previously existing cystic disease and benign tumors are known factors in the development of these neoplasms. Bittner's excellent work on the milk factors in mice has not been proven in the humans as yet, because the time factor involved in studying generations of human beings. Trauma to the breast often results in fat necrosis which clinically simulates carcinoma, but trauma, per se, has never been considered a great etiological factor.

Although many classifications of mammary carcinoma have been put forward, none are acceptable to clinicians and pathologists alike. Attempts at grading these tumors have met with acceptance in most quarters.[12,26,27] The type of cellular structures composing the tumor and the behavior of the tumor as regards metastasizing will give a rather accurate prognosis. For this reason, immediate biopsy of any suspicious lesion of the breast and a meticulous search for regional and distant metastasis should be undertaken. Various methods of biopsing lesions of the breast have proven to be accurate. The employment of aspiration biopsy by the Memorial Hospital group in New York[2] has given satisfactory results in their hands. By this method the type of cells present are determined, but it is impossible to obtain information regarding the relationship of various structural components in this procedure. Many men deprecate incising a wedge-shaped portion of the tumor for microscopic study because of the fear of spreading cancer cells into channels where they might rapidly disseminate. However, Haagensen believes no harm results if incision into the tumor is carefully done. Complete excision of the tumor, with a portion of surrounding normal breast tissue, has been a certain, accurate method that has given the surgeon ample opportunity to study the tumor grossly at the operating table. The correlation of the gross ap-

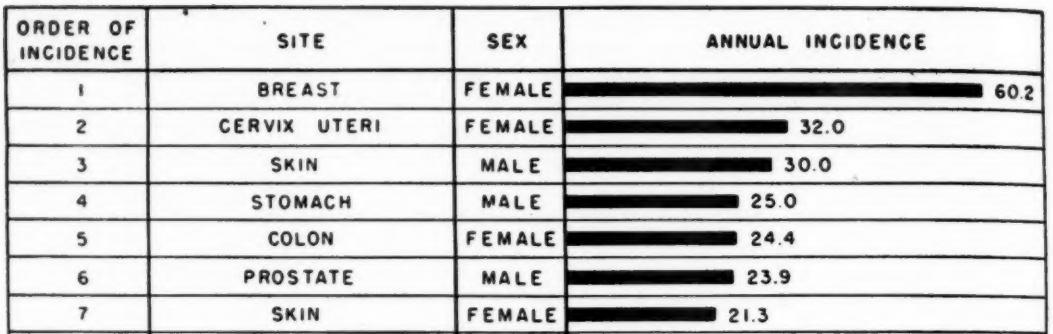


Fig. 1. Average annual cancer incidence rates per 100,000 population, New York State, exclusive of New York City, 1942 to 1947.

pearance of the tumor, with the reported microscopic findings, will give the greatest information about the type of lesion present. Indeed, many men believe the gross appearance of the tumor will give more information than frozen microscopic sections of the tumor.[8] If there is doubt as to the type of pathology present, many sections should be studied from paraffin sections to arrive at a correct diagnosis. There is not much evidence that removal of a malignant tumor, with a wide margin of tissue, several days before radical operation exerts any deleterious effects.

Once a correct pathological diagnosis has been made and the extent of metastasis determined an attempt should be made to erradicate the cancer, if possible. If the disease process has spread to the skeleton, lungs or other distant points; if the skin over the breast is extensively involved; if there is edema of the arm, palliative treatment is recommended. If the cancer is confined to the breast and the adjacent axillary nodes an attempt should be made to remove completely the cancer by radical surgery. One should keep in mind, that as of today, radiation[5] and surgery[21,24] are the only proven methods of dealing with breast cancer. The literature[14,15,17,26] abounds with statistics regarding five-year survival rates for each method and for a combination of both. Most claims for each of the methods will be decided in the future.

Radiation, by means of radium needles, has been reported by Keynes[19] as being successfully used in treating cancer of the breast with axillary metastasis. McKittrick[22] in this country attempted to repeat Keyne's results, but has now abandoned this treatment in favor of radical surgery.

McWhirter of Edinburgh[23] has recently published some rather astonishing five-year survival rates, in which simple mastectomy was carried out for carcinoma of the breast with axillary metastasis, leaving the axillary nodes to be treated post-

operatively with heavy doses of radiotherapy. He bases the rationale of this treatment on his belief that the axilla cannot be freed of all cancer with surgery. It is a well-known fact that radiotherapy can cause extensive fibrosis in which cancer cells are "locked up" for many years, but never thorougly destroyed. Time will disclose whether or not there is a place for this type of combination therapy in the treatment of cancer of the breast.

Simple mastectomy alone, unfortunately, is still done by some surgeons who have a defeatist attitude regarding this disease. By doing this limited surgical procedure the surgeon foregoes the opportunity for his patient to participate in the excellent five-year survival rate statistics that have come forth following radical mastectomy. About 60% of patients with cancer of the breast have axillary metastasis when first seen. These patients in which the disease is limited to the axilla should have a classical radical mastectomy in which sufficient time is taken to dissect out meticulously all nodes high in the axilla, supraclavicular space and other lymphatic pathways. The work of Halsted, Willy Meyer, Greenough,[28] Rodman and others layed the foundation as to what constitutes a radical mastectomy. By utilizing many of the facilities available today such as anesthesia, blood transfusions, antibiotics and others, the operability rate has been extended. Today, radical mastectomy, as advocated by Adair, Pack,[25] Haagensen, Cole and others, offers the patient with cancer of the breast a better chance for cure than ever before. More patients are given this chance as the operability rate now approaches 75%. A few surgeons have attempted more adventuresome surgery in which they have attempted to remove the nodes within the thorax, elevate the clavicle, and routinely do an extensive neck dissection. Their experience has been limited to very few cases and the benefits derived from these extensive procedures is still doubtful.

The value of preoperative and postoperative radiation[21] has been a debateable subject for years. At the present time, preoperative radiation has been dispensed with by most men, but postoperative radiation is still being used in an attempt to "lock up" in dense fibrous tissue any remaining cancer cells, and to prevent local recurrences over the operative site and axilla.

Radiation has a definite place in the treatment of metastasis. Its role here has definite value and should be started when the patient complains of pain which so often is the first symptom of bony metastasis. Radiation should be started even before the metastatic lesions are demonstrated by x-ray. Relief is often spectacular and often gives the patient months and sometimes years of comfort.

Attempts to influence the course of breast carcinoma by changing the hormone balance in the patient has been accomplished by doing routine castrations,[18,29] either by surgery or radiation, on all patients with breast carcinoma. This was first done because of the known rapid growth of carcinoma of the breast during pregnancy. It is the routine procedure in most clinics to give irradiation to the ovaries.

Hormonal therapy in the form of androgen and estrogen has been given a thorough trial in many clinics[13] during recent years. At the present time, it would seem to be a valuable supplemental type of treatment in treating metastasis. It often gives the patient a feeling of well being which at times extends over a period of months.[2] Androgen seems to be of greatest benefit to women under sixty years of age in which irradiation to painful bony metastasis no longer gives relief. Some rather startling results have been recorded when used in this manner. Estrogen gives most benefit to women over sixty years of age when the metastasis in soft tissue no longer can be controlled by radiation.

In conclusion, it should be stated that if women can be educated in self-examination of their breasts and present themselves early to their physician and receive adequate radical surgery, even better results will come forth in the future.

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## THE USE OF METHANTHELINE BROMIDE (BANTHINE) IN PEPTIC ULCER AND OTHER GASTROINTESTINAL DISORDERS

*(Continued from Page 640)*

The maintenance dose must be adjusted to each individual case, remembering that night control is still of fundamental importance.

3. *The unnecessary use of Banthine.* In self-limited conditions such as the acute diarrheas and in irritable bowel cases in which the regulation of the patient's life and habits, his general hygiene and his diet is of more fundamental importance, Banthine is not needed.

4. *The use of Banthine in the face of obvious contraindications* such as those previously mentioned. Irreparable damage can at times be done in this way and it behooves us to survey each patient carefully for abnormalities which contraindicate its use.

Finally, it is only by the judicious use of Banthine that its value to our patients can be enhanced. This drug is still in its infancy. It is only by carefully evaluating its effect in each individual case that its ultimate place in therapeutics can be established.

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# INTERRELATIONSHIPS BETWEEN CARDIAC AND PULMONARY DISEASES

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Minneapolis, Minnesota

BECAUSE of the close anatomic and physiologic relationship between the heart and the lungs, it is to be expected that disease of one organ will produce an effect upon the other, and that this may often lead to difficulties in diagnosis. Dyspnea is the commonest symptom in diseases of the heart and yet this symptom is pulmonary in origin. Diseases of the lungs may lead to right heart enlargement and failure and be confused with primary disease of the heart. If pitfalls in diagnosis are to be avoided, it is important to understand the changes in the lungs produced by heart disease, and, conversely, the effect of pulmonary disease upon the heart.

Heart disease produces changes in the lungs by alterations in the pulmonary vascular pressure. Under normal circumstances the pressure in the vessels of the lungs is low. The mean pressure in the pulmonary artery of a normal man is 15 mm. Hg and the capillary pressure 9 mm. Hg. Failure of the left ventricle associated with systemic arterial hypertension or aortic valve disease leads to a sudden rise in pulmonary vascular pressures. If the pulmonary capillary pressure exceeds the colloid osmotic pressure of the blood, pulmonary edema ensues. These changes in the lungs are responsible for the familiar symptom of dyspnea. The combination of dyspnea, cardiac enlargement together with the typical findings of pulmonary edema, usually makes the diagnosis simple. Occasionally the atypical nature of the pulmonary edema in the roentgenogram of the chest may lead to confusion in diagnosis. The edema may be confined to one area of the lung simulating pneumonia. This may be particularly confusing if cardiac enlargement is absent as may be true in myocardial infarction with associated left ventricular failure.

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Read before the annual meeting of the Minnesota State Medical Association, Minneapolis, Minnesota, May 26, 1952.

Mitral stenosis produces chronic pulmonary hypertension. This is to be expected as the interference with the flow of blood from the lungs into the heart is caused by a mechanical obstruction rather than to changes in the efficiency of the cardiac musculature. Acute attacks of pulmonary edema may occur as in left ventricular failure but more commonly a different clinical picture is seen. The patient will complain of chronic exertional dyspnea which is oftentimes associated with cough and hemoptysis. These patients will have marked elevation of the pressure in the pulmonary arteries. Microscopic sections of the lungs will show thickening of the alveolar septa and hemosiderin-filled macrophages in the alveoli. Because the murmur of mitral stenosis is readily overlooked, the symptoms are often wrongly attributed to bronchitis or bronchiectasis. The appearance of the roentgenogram of the chest may lead to confusion. There may be a reticular appearance to the lung simulating a fine pulmonary fibrosis or an appearance resembling miliary tuberculosis. This roentgenographic picture has been called hemosiderosis of the lungs.

An accumulation of fluid in the pleural cavities is a common accompaniment of congestive heart failure. The fluid is usually bilateral, although it may be more marked on the right. Occasionally marked unilateral hydrothorax occurs as a complication of heart failure. This may not be accompanied by peripheral edema. Under these circumstances, the pleural fluid may be falsely attributed to tuberculosis or bronchogenic carcinoma.

Dilatation of the pulmonary arteries is commonly seen with pulmonary hypertension complicating heart disease but is usually moderate in degree. With certain types of congenital heart disease the dilatation may be enormous. This is particularly true in auricular septal defect which is associated with a marked increase in pulmonary blood flow. Dilatation of the major trunks of the pulmonary artery may complicate pulmonic stenosis or may occasionally occur as an isolated anomaly.

Pulmonary infarction is a common complica-

tion of congestive heart failure. It should be suspected whenever a patient with cardiac disease complains of chest pain or hemoptysis. At times the only clinical manifestation may be a worsening of the symptoms of heart failure. The roentgenographic picture of pulmonary infarction is often confused with or obscured by pulmonary edema and hydrothorax.

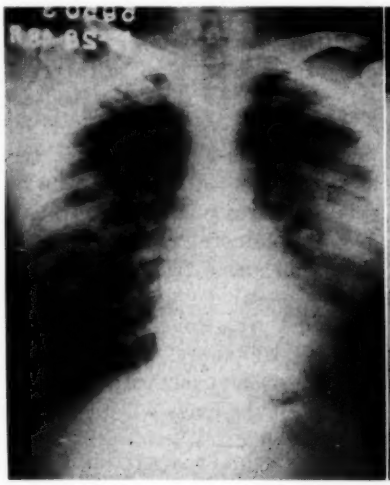

Fig. 1. Hypertensive heart disease with pulmonary edema.

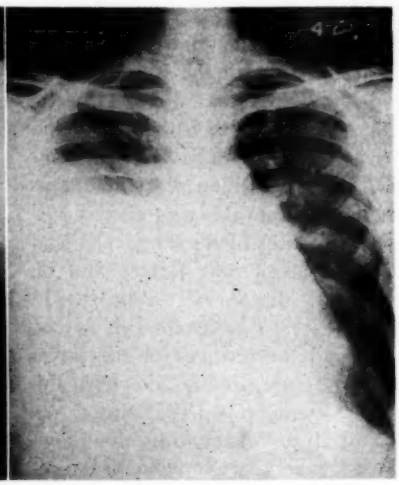

Fig. 2. Mitral stenosis with unilateral hydrothorax.

Localized diseases of the lung such as pulmonary tuberculosis, lung abscess, bronchogenic carcinoma or bronchiectasis produce little effect on the heart. This is because these diseases produce no elevation of pulmonary arterial pressure. On the other hand diffuse diseases of the lung such as pulmonary emphysema and diffuse pulmonary fibrosis commonly lead to pulmonary hypertension, right heart enlargement and right heart failure.

Pulmonary emphysema is the most common disease of the lungs which leads to right heart enlargement and failure. It is of particular importance because of the frequency with which it is confused with primary disease of the heart. Dyspnea is the most prominent symptom. At first the dyspnea occurs on exertion but later dyspnea may be present at rest particularly when bronchial infection is present. The dyspnea is in no way related to involvement of the heart but rather is caused by the disease process in the lungs. As a result of the loss of the normal elastic forces of the lungs the residual air is markedly increased with a corresponding reduction in vital capacity. In addition there is obstruction to flow of air in and out of the lungs as a result of the alteration in architecture of the lungs and the associated bronchial infection. In the latter stage of the disease there is marked interference with ventilation of the alveoli resulting in anoxia and retention of carbon dioxide. This interference with the respiratory function of the lungs is the eventual cause of death.

The development of pulmonary hypertension in emphysema is variable. Almost all patients with severe emphysema will have some elevation in pulmonary arterial pressure, but severe pulmonaary hypertension occurs in a minority. Marked pulmonary hypertension occurs most commonly in those patients with severe anoxia and there is reason to believe that the anoxia may play a part in the production of the pulmonary hypertension.

Evidence of right heart enlargement is best obtained from the electrocardiogram although caution must be exercised in interpretation because of the positional changes which are commonly present. Evidence of gross cardiac enlargement on the roentgenogram of the chest is usually absent except in the presence of marked right ventricular failure. The circulation time is usually normal even in the presence of right heart failure. This is because the cardiac output is normal or even increased.

The diagnosis of right heart failure in patients with emphysema is often frought with difficulty

and uncertainty. As mentioned previously dyspnea and cyanosis are symptoms of the pulmonary disease and are in no way related to heart failure. Edema of the lower extremities is commonly seen in pulmonary emphysema. The edema does not always seem to be related to cardiac failure. Often it results from prolonged dependency of the legs. Because of the severe dyspnea the patients may remain in a chair with the legs dependent day and night. Under these circumstances one would expect some edema of the legs. The size of the liver is often difficult to evaluate because of the low diaphragms and this further complicates the diagnosis of right heart failure. The most reliable criterion of right heart failure would appear to be a definite elevation of the venous pressure.

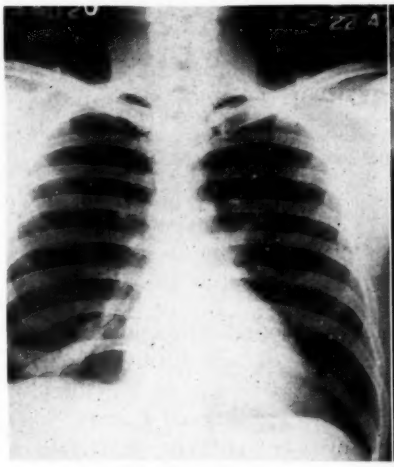

Fig. 3. Pulmonary infarction complicating congestive heart failure.

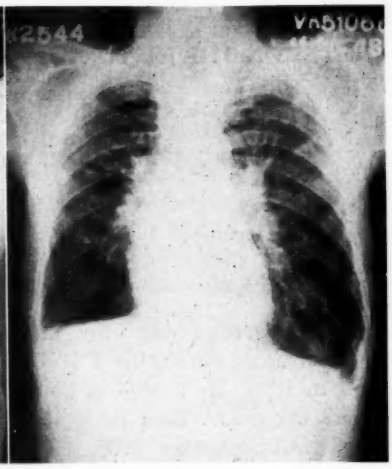

Fig. 4. Severe pulmonary emphysema with cor pulmonale.

In the differential diagnosis of primary cardiac and primary pulmonary disease symptoms are of little value. Exertional dyspnea, nocturnal dyspnea, orthopnea, and edema may occur in both. Physical findings are of greater aid. Severe cyanosis should always suggest primary disease of the lungs or congenital heart disease with a right to left shunt. A barrel chest with limited motion and low diaphragms is usually found in pulmonary emphysema. The determination of cardiac enlargement on physical examination is of great aid. If the heart can be determined to be markedly enlarged by palpation of the apex impulse or percussion it is safe to ascribe the symptoms to primary heart failure. On the other hand if the apex impulse cannot be felt and cardiac enlargement cannot be detected by percussion one should strongly consider the possibility of the symptoms being on the basis of pulmonary disease. The roentgenograms of the chest must be interpreted with caution. In silicosis or sarcoid with extensive pulmonary fibrosis the disease of the lungs is obvious, but pulmonary emphysema may be difficult or impossible to diagnose from the roentgenogram. The size of the heart is of aid, as marked cardiac enlargement does not usually occur with pulmonary emphysema even in the presence of cor pulmonale. If cardiac enlargement is present it is right ventricular in type. The electrocardiogram is useful in that there is evidence of right ventricular enlargement in cor pulmonale whereas most types of acquired heart disease except mitral stenosis show evidence of left ventricular enlargement.

Finally, mention should be made of the use of the measurement of vital capacity in diagnosis. This is an extremely simple procedure which can be performed with an inexpensive portable apparatus.* In congestive heart failure the vital capacity is moderately reduced but extreme reduction is uncommon unless marked pulmonary edema or hydrothorax is present. Moreover in performing the vital capacity the patient can expel the air with moderate rapidity. In severe pulmonary emphysema with cor pulmonale the

*(Continued on Page 702)*

*Manufactured by the McKesson Appliance Company, Toledo, Ohio.

# History of Medicine In Minnesota

## NOTES ON THE HISTORY OF MEDICINE IN WASECA COUNTY PRIOR TO 1901

B. J. GALLAGHER, M.D., and J. F. LYNN, M.D.

*(Continued from the June issue)*

**Homer P. Dredge** was born in Pleasant Mound Township, Blue Earth county, Minnesota, on August 3, 1870. He graduated from Rush Medical College, Chicago, in 1896. He located in Janesville, Waseca County, in June of 1896 and was there one year. Then he located at Bellview, Redwood County, where he remained until September, 1903, when he moved to Sandstone, Minnesota, where he still is in practice (1952).

He was married at Duluth to Miss Elma H. Freeman. Six children were born of this union, and all are living now in 1952. They are: Ethel Freeman Dredge, Librarian, Minneapolis; Florence Isabel Dredge, now the wife of Judge Earl J. Lyons, Minneapolis; Lieutenant Colonel Thomas Everett Dredge, M.D., at present on service with the army in Korea; Alice Hazel Dredge, now Mrs. Paul R. Wylie of Montana; Homer P. Dredge, a graduate of pharmacy from the University of Minnesota, and owner of a drug store at Waverly, Minnesota; Robert Morris Dredge, an employe of the National Cash Register Company and now living in Richfield, Minnesota. Dr. and Mrs. Dredge have twelve grandchildren.

**M. S. Gove,** the first actively practicing physician in Waseca County, was born in the town of Strafford, Orange County, Vermont, in 1829. He studied medicine in his native state, graduating in 1849. He then came west to Indiana, where he practiced until 1858, when he came to Minnesota, taking up his residence in Wilton, then the county seat of the one-year-old county. He was a public spirited man and took a great interest in all public matters. In 1859, he was elected County Commissioner, and became Chairman of the Board at its first meeting after the election. At one time, he was County Superintendent of Schools. When the Waseca County Anti-Horse-Thief Society was organized in 1864, he was its first President, and was very active in it until his death ten years later. The organization is still in existence in the county and has members down through the fourth generation. After his death, the Society resolved:

"That we will ever cherish his memory with feelings of consideration and respect as a man of scholarship and ability in his chosen profession, a kind neighbor and a good citizen."

His professional cards appeared in the first and all the subsequent issues of the *Waseca Citizen,* which was started in Wilton, in 1860. They seem rather modest, in view of the fact that so far as is known, he was the only regular physician in the county at the time:

M. S. Gove, M.D.
Physician, Surgeon and Obstetrician
Office Broadway, next door west, Wilton House
Wilton, Minnesota

Conversant for 14 years with disease experience in hospitals and 10 years extensive practice in the west, may entitle him to a portion of the patronage.

Since he was asking for a "portion of the patronage" it would seem that he must have had competition of some kind.

He married Miss Sarah Dodge, then a teacher in the public schools of the county. They had no children.

When the town of Waseca started in the fall of 1867, after the arrival of the railroad and a movement was on soon to move the county seat to Waseca, Dr. Gove fought for its retention in Wilton. When Waseca became the county seat at the election of 1869 and Wilton was left high and dry, five miles from the railroad, he surrendered to the inevitable and moved to Waseca in 1870.

Late in November, 1874, he contracted an infection in one hand in the line of professional duty and died a few days later, on December 1, 1874. He is buried in a lonely and isolated cemetery about one-half mile south of the old Wilton Townsite.

**Frank Winston Greene** was born in Baltimore, Maryland, on October 5, 1853. Later his parents moved to Boston, where he grew up and went to a physicians and surgeons preparatory school, and later came to Minnesota, where he graduated from the Minnesota College Hospital in 1887. He received his Minnesota license on March 12, 1887 (1319R). At first he located in Minneapolis but in 1890 he is listed as practicing in Benson, Swift County, Minnesota, and in 1893 at Langford, South Dakota. In 1894 he came to New Richland, Waseca County, and there he lived until 1904. When Dr. Charles Dolan of Waterville moved to Worthington (after the sudden death of his brother, Dr. Edward Dolan, who had been in practice there), Dr. Greene moved to Waterville, Le Sueur County. He remained there until 1909 or 1910, when he moved to Seneca, South Dakota. In 1912, he moved to Bruno, Minnesota, and died there on April 17, 1934. He was buried at Waterville.

In 1887, he married Miss Katherine Rourke. They had two children, a son Winston D., born in 1896 and who died in 1905 at Waterville, and a daughter, born in 1904 at Waterville. She is now Mrs. O. E. Eklund, wife of the president of the State Bank of Bruno, Minnesota. They have one son, age 19 years, who is a student at Hamline University. Mrs. Greene died in Bruno in 1941 and is buried at Waterville, Minnesota.

**David W. Horning** filed his certificate (dated January 28, 1884) in Waseca, April 5, 1884. We have been unable to learn anything further about him here, but the Wabasha County notes in the November, 1944, issue of MINNESOTA MEDICINE, state that:

"He graduated from the Homeopathic Medical School of Chicago in 1883. He practiced in Lake City until 1891, when he moved to Minneapolis."

He practiced in Waseca only for a year or two in 1884 and 1885, before moving to Lake City, and later in 1891 to Minneapolis. Nothing further is known about him.

**William E. Hubbard,** a physician of the regular school, was graduated at Rush Medical College in 1885. He received his license in Minnesota on October 27, 1885. His name is on the list as being located in Waseca about 1890, and he is remembered by at least one old-timer. He seems not to have registered his certificate with the Clerk of Court. He probably was not in Waseca for very long, and nothing further is known about him.

**Eugene Hubbel,** a homeopath, was graduated from the Hahnemann Medical College in 1883 and received his Minnesota license on September 18, 1884. He was located at Clearwater, in Wright County, for several years. In March, 1889, he moved to Waseca where he practiced for about a year. An old timer who remembers him, recalls that he made his calls on a high-wheeled bicycle. From 1893 until at least 1902, and probably for many years after that, he practiced at Saint Paul. He died in one of the Twin Cities only a few years ago.

**Frederick N. Hunt** is listed in the Clerk of Court's office in Waseca as having filed his certificate dated April 8, 1884, on June 10, 1892. He is listed in *Child's History* in 1893, as being one of the stockholders and the first cashier of the newly organized Citizens State Bank (now the First National). A personal communication from his son states that he went to Waseca from Fairmont for a year in 1892-1893, to help his uncle start a bank, that he did not practice in Waseca but went to Blue Earth in 1893, where he practiced until 1914, and then went to Fairmont. He is written up at length in the "History of Medicine in Martin County," MINNESOTA MEDICINE, October, 1942.

**M. V. Hunt** was one of the leading physicians of Waseca for many years. He was born in Darke County, Ohio, in 1848. He received his early education in Anderson, Indiana, where his parents moved when he was a child. He pursued his studies in Earlham College at Richmond, Indiana, where he graduated in 1867. He then matriculated at the Medical College of Cincinnati, Ohio, graduated March 4, 1872, and commenced practice at Anderson, Indiana. After a few months there, he removed to Janesville, Minnesota, and eighteen months later came to the city of Waseca. In the fall of 1879, he was elected County Superintendent of Schools, and he also served as County Coroner. He was a man of great natural ability, heightened by a superior education. In March, 1876, he married Miss Addie A. Andrews who died in July, 1887, leaving one child. He practiced in Waseca until about 1888, when he moved back to Anderson, Indiana. The date of his death is not known to us.

**Attila M. Hutchinson,** a homeopathic physician, was born in LeRoy, Gennessee County, New York, in 1847. When he was five years old his family moved to Fond Du Lac, Wisconsin, and there he was reared. He began the study of medicine at an early age, having a natural bent in that direction. Later he attended the Hahnemann Medical College, Chicago, where he graduated in 1877. He came to Waseca in April, 1885. While attending college, it is a matter of record that he took the first prizes on the "Theory of Practice of Medicine," and on "Diseases of the Heart and Lungs." In 1872, he married Miss Libby P. Otis of Wisconsin. They were the parents of five children. He was a member of the Minnesota Homeopathic Institute and also of the Ancient Free and Accepted Masons. He was in Waseca for a few years but it is not known just when he left or where he went.

**L. E. Kuchenbecker,** whose Minnesota license was dated October 12, 1893, filed it in Waseca July 7, 1900. We have been unable to find his name on any other list. Dr. J. F. Lynn, who came to Waseca in the fall of 1900 and is still practicing, does not know of him.

**William A. Lang**—the Freeborn County notes in the February, 1949, issue of MINNESOTA MEDICINE had this brief note only:

"Dr. Lang located in Hartland (in Freeborn County, three or four miles south of the Waseca County line) in 1890. In 1891, he moved to New Richland (Waseca County) but came to Hartland every Thursday."

In *Child's History* of Waseca for the year 1886 it is stated that Dr. W. A. Lang was appointed County Physician for the Fourth District, so he must have been in New Richland at that time. Also in a public Medical Directory for 1886, 1890 and 1893, he is listed as a physician in Waseca County. He was a physician of the regular school and graduated from McGill University Medical Department at Montreal in 1881. It is thought that he left New Richland in the late 1890's. An edition of the *New Richland Star* in 1886 has this note:

"Dr. W. A. Lang, graduate of a Montreal Medical College, located here about two years since, has by his skillfulness in his profession and his careful attention to the minor complaints, secured a firm hold upon the confidence of our citizens, and has a reputation second to none."

Nothing more is known about him.

**James B. Lewis** was born in Lancaster, Pennsylvania, December 18, 1855. Later the family moved to Reading, Pennsylvania. He graduated from the Medical Department of the University of Pennsylvania in 1878. He came to Minnesota in 1885, and was licensed on November 7, 1885 (1123R). He located in Saint Paul, and on June 16, 1886, he married Miss Lily B. Lienau of Saint Paul. They had a son and a daughter, both living in South Saint Paul at the time of this writing (1952). The daughter, Marguerite (Mrs. S. B. Ferguson) is Executive Secretary of Family Service of South Saint Paul; the son, Charles S. Lewis, is retired.

In 1894, the Lewis family moved to Waseca, where Dr. Lewis practiced until 1900. Then he moved to St. James, where he remained until 1910, when he located in South Saint Paul. After that he was Coroner of Dakota County for three terms.

The later years of his life were spent in semi-retirement. He traveled a great deal. He was an ardent sportsman, doing much hunting, but as he grew older gave that up for the milder sport of fishing. On July 27, 1924, he died in his sleep while on a fishing trip on Whitefish Lake, Jenkins, Minnesota. He was buried in Acacia Park Cemetery, Mendota. He was a member of the Episcopal Church, the Masons, and the Ramsey County, Minnesota State and American Medical Associations.

**James F. Lynn** was born in Loudoun County, Virginia, April 20, 1871. He received his primary education in the country schools, three miles from his home. He went then to William and Mary College at Williamsburg, Virginia, after which he taught a country school for two years. He then took academic courses at the Richmond College, preliminary to pursuing the study of medicine at the University College of Medicine, Richmond, where he finished with distinction in 1896. Later he continued his medical studies in New York at the New York Polyclinic and Hospital where he received advanced degrees. He practiced medicine in

Richmond for two years, at the same time acting as demonstrator of anatomy at the University College of Medicine.

He came to Waseca in August, 1900, and established the practice of medicine, which he is carrying on at the present time (1952).

Several years ago, a friend wrote the following tribute to Dr. Lynn:

"Dr. Lynn is steadfast and loyal, having the confidence of businessmen, laboring men and farmers. He has been a success and a leader in his profession. As a physician, he has been a leader in health work in his community. He has been president of the Waseca County Medical Society at different times. In May, 1917, President Wilson appointed him medical member of the Waseca County Draft Board. These duties he faithfully performed at a great sacrifice to his medical practice. This work he continued for over a year, until the need for doctors in the Overseas American Army became so great that he resigned and enlisted. He was immediately appointed Captain in the Medical Corps, and after a brief training in the United States, he was sent overseas to France. There he served as Chief of the Medical Service with Base Hospital 107 A.E.F., until his return to the United States in June, 1919. He was released from the army with a honorable discharge July, 1919.

He helped to organize and was one of the charter members of the Waseca American Legion Post. In 1922 and also in 1928, he was the Democratic nominee for Congress in the First Minnesota District. In both campaigns he put up a courageous, militant fight, and while not elected (this district being a stronghold of the Republicans) he made a creditable showing, each time receiving more votes for that office than any other Democrat had ever done before or since. All this was done at a great personal sacrifice. It cost him a lot of money and he lost a lot of time from his business. He was one of the twenty-one Minnesota delegates elected to the Constitutional Convention for the repeal of the 18th Amendment. He was Chairman of the Roosevelt Business and Professional League for Waseca County; Chairman of the Roosevelt and Garner Club for the city of Waseca; and Chairman of the Waseca County Democratic Committee for two years. He has also served as a member of the Waseca School Board and Chairman of the Waseca Charter Commission. These are not all the things he has engaged in for the good of the community, the State and the Nation, but it is sufficient to give you at least in part the picture of the kind of man he is."

*The Genealogy of James F. Lynn, M.D.*

Great, Great Grandfather, John Lynn.....born 1729

Great Grandfather, Fielding Lynn.....born 1763
died 1794

Great Grandmother, Ruth Fristoe Lynn. .....born 1772
died 1833

Grandfather, James Fristoe Lynn.....born 1806
died 1864

Father, Bushrod Washington Lynn.....born 1842
died 1917

Mother, Frances Allen Lynn.....born 1844
died 1908

Dr. James Fristoe Lynn.....born 1871

He married Miss Jessie Helms on January 28, 1904, and they have two sons. James F. is married, lives in Owatonna, and has three children. Robert Lee is married, lives in Saint Paul, and has two children.

Dr. Lynn's hobbies are riding horses and photography. He is still City Health Officer for Waseca (1952).

*(To be Continued in the August issue)*

# President's Letter

## PUBLIC HEALTH—MEDICINE'S EXTRA EYE

Just as many mothers sometimes need three arms to accomplish all their duties, so medicine needs an extra "eye" to keep watch over the health of the nation's people. The field of public health has long offered that extra "eye" for doctors of medicine.

The benefits from action in the interest of public health have been of extreme value to the medical profession as well as the public. Doctors of Minnesota will again have an opportunity to avail themselves of latest scientific developments in public health this October, when the sixth annual Minnesota Public Health Conference will convene. The dates are October 2 and 3, and the place is the Saint Paul Hotel.

Anyone who has attended the previous conferences, knows from first-hand experience, that their opportunities are many and varied.

The Minnesota Public Health Conference, an official affiliate of the American Public Health Association, provides a forum for the discussion of vital public health problems. It brings together representatives of medicine, nursing, dentistry, pharmacy, engineering, and veterinary medicine. The continuing co-operation and participation of these groups have helped make the conference an extraordinarily successful means of pin-pointing problems and emerging with machinery to resolve them.

A resolution promising the medical profession's aid and support in this conference was passed at the 1951 House of Delegates' meeting. Thus, we have a vital stake in the public health conference, not only through the working organizational committees, House of Delegates, officers and Council of the Minnesota State Medical Association, but through the individual physicians of the state as well.

I should like to urge physicians of Minnesota to do their part in keeping that extra "eye"—public health—an alert one. Its sharpness depends greatly on participation and co-operation from the medical profession. The Minnesota Public Health Conference should be a "must" on the calendar of all public-minded doctors. It will be concrete evidence of your continuing efforts to improve the already high health standards for the people of your state and nation.

Roger L. J. Kennedy

President, Minnesota State Medical Association

# Editorial



## DIRTY POLITICS—H.R. 7800

IT seems worthwhile to relate the sequence of events that led up to the defeat by Congress of the bill designated as H.R. 7800. The story is an example of tricks that are played to get bills passed without due deliberation—bills which, if passed, would give added power to the powers that be and, if defeated, would afford an opportunity to discredit the opposition. This can be correctly termed—dirty politics.

A bill to amend Title II of the Social Security Act was introduced in Congress on Monday, May 12, 1952, and referred to the House Committee on Ways and Means. Printed copies of the bill were not available until Wednesday, May 14. The bill was considered immediately by the committee and reported favorably on Friday, May 16, without public hearings and with the request that action be taken on Monday, May 19, under suspension of rules. This meant that debate was to be limited to forty minutes and no amendments were to be allowed. Such undue haste should have been enough to have aroused suspicion and investigation. It did.

The bill provided for an increase in old age and survivors pensions. However, Section 3 of the bill provided that the Federal Security Administrator (Oscar Ewing at the present writing) should: (1) provide by regulation when and where physical examinations should be taken; (2) be authorized to prescribe the examining physician or agency; and (3) establish the fees. Quite an addition to the considerable authority already invested in the Federal Security Administrator.

While the bill did not establish permanent and total disability benefits, it established a precedent and framework for the adopting of such benefits in the future. In view of this dangerous precedent and the immediate control which Section 3 of the bill would vest in the Federal Security Administrator, the AMA opposed its adoption.

The AMA did not object to the portion of the bill which provided for an increase in Social Security payments, but it did object to Section 3 which would have put the government's foot in the door of socialized medicine.

The facts indicate that a sneak procedure was used by the Social Security Agency to get Section 3 "written in" an otherwise acceptable bill.

The AMA was taken to task by President Truman for having defeated the bill which would have increased payments in Old Age and Survivors Insurance benefits. This was probably true, for when the undesirability of Section 3 was called to the attention of Congress, the bill failed to pass by a two-thirds majority required under the suspension of rules.

Unless the story of bill 7800 is known, the opposition of the AMA might well put the physicians of the country in an unfavorable light in the eyes of Old Age and Survival beneficiaries. A statement by the AMA secretary let it be known that the AMA would not oppose a bill providing in a straight-forward way for an increase in payment to Social Security beneficiaries with no trick riders. The same bill was resubmitted and passed by the House with only twenty-two adverse votes. The bill is still opposed by the AMA, and it is to be hoped will be killed in the Senate.

## STATE MEDICAL ASSESSMENT

THE House of Delegates at its meeting May 26, 1952, during the annual meeting of the Minnesota State Medical Association, voted to assess each active member $10 for the year 1952, effective immediately.

The association has been calling upon its reserves since 1949, in larger amounts each year, so that it has little reserve left. The dues have not been sufficient for the needs incident to the expanded field of activities. Provision for scholarships of $1,000 a year for medical students from communities of less than 5,000 population will soon add $4,000 yearly to the association's expenditures. Inflation has practically doubled the office salary item. An important factor in the picture is the reduction in membership from 3,100 as of January 1, 1950, to about 2,600 as of May 1, 1952, due to many physicians taking advantage of the non-dues paying life membership and the large number temporarily serving in the armed forces.

A letter from the state office which has gone out to each member calls attention to the fact that the new assessment of $10 added to the present $30 is still less than the dues of $50 paid in Iowa, Nebraska, North and South Dakota and the $60 paid in Wisconsin.

The assessment is payable at once directly to the Minnesota State Medical Association office at 496 Lowry Medical Arts Building, Saint Paul 2, Minnesota.

## TREATMENT OF RHEUMATIC FEVER

MUCH has appeared in the literature regarding the use of ACTH and cortisone in the treatment of rheumatic fever. Editorial mention* has been made of the apparent prompt abatement of the symptoms and laboratory evidence of activity of the disease following the use of these two drugs but that their affect on the over-all picture of the heart disease frequently accompanying the disease had yet to be proved. A warning was issued against the indiscriminate use of the two drugs.

The question of practical importance as to whether ACTH and/or cortisone should replace the salicylates in the treatment of rheumatic fever has apparently not yet been settled. According to a recent release of the American Heart Association the remedies mentioned have been and are being studied in some thirteen research centers in the United States, Canada and Great Britain in a co-operative effort to evaluate the new drugs in comparison with the salicylates. Funds for the study have been supplied by the National Heart Institute of the U. S. Public Health Service, the British Research Council, the American Heart Association, the Canadian Arthritis and Rheumatism Society and various hospitals and medical centers. The ACTH has been supplied by Armour and Company and cortisone by Merck and Company.

The study has been going on since January, 1951, and the preliminary report on the first 302 of the 658 patients studied states that there is no difference in the time required for the acute symptoms to subside after the administration of ACTH, cortisone or aspirin and no conclusions are so far justified as to the drug most effective for the control of the acute illness. No information is yet available on the comparative effectiveness of the three drugs in preventing chronic heart disease.

Until some proof is forthcoming that ACTH or cortisone are superior to the salicylates in the treatment of rheumatic fever and until their side effects are better understood, the practitioner would seem justified in adhering to the salicylates for the treatment of this disease and leaving further trial of ACTH and cortisone to the research centers.

*Editorial: The need for early diagnosis in rheumatic fever. Minnesota Med., 34:164 (Feb.) 1951.

## DR. LAWRENCE RETIRES

A TESTIMONIAL dinner was given Dr. Joseph S. Lawrence, retiring head of the legislative office of the AMA in Washington, on Sunday, June 8, at the Palmer House in Chicago. Some 200 officers of the AMA and state medical associations attended the dinner in honor of the physician who for the past eight years has held a difficult assignment and has conducted it in a dignified and effective manner. Starting with an office consisting of one room and one employe, it now has a personnel of sixteen.

Dr. Lawrence had a background of twenty years of legislative experience in New York State as a representative in Albany of the State Medical Association. His office in Washington was first under the Committee of Public Education of the AMA. Later it became directly responsible to the Board of Trustees before being placed under the Committee on Legislation, headed first by Dr. Dwight Murray and now by Dr. Blasengame of Texas.

The AMA office in Washington has been accused of being a doctors' lobby. As a matter of fact, the office is a two-way information bureau, supplying information on legislative matter to the profession throughout the country and medical viewpoints to anyone in Washington who requests them. The office is in no sense a lobby. According to Dr. Lawrence's own statement, he has never asked any legislator to vote for or against any measure.

Dr. Lawrence deserves the thanks of the profession for having handled a difficult assignment well.

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Physicians can stimulate community participation in X-ray surveys by setting a good example themselves. It would be gratifying if every hospital required that staff members have a chest X-ray, at least twice a year. The Children's Memorial Hospital is the first Chicago hospital to make such staff requirement. This example should be followed voluntarily by every hospital in the country. EDWARD A. PISZCZEK, M.D., *The Illinois Med. J.*, March, 1952.

# Medical Economics

**Edited by the Committee on Medical Economics**
**of the**
**Minnesota State Medical Association**
**George Earl, M.D., Chairman**

## FINAL APPROVAL GIVEN SCHOLARSHIP PLAN

A working plan for administering the Minnesota State Medical Association's Rural Medical scholarship fund was given final approval at the annual meeting in Minneapolis in May. The plan, main purpose of which is to assure at least one rural practicing physician a year to areas of Minnesota, was discussed and approved by the House of Delegates.

A special committee appointed to work out details of the plan of operation reported to the House of Delegates. In presenting a brief outline of the plan, the report stated:

"The scholarship will consist of a grant of one thousand ($1000) dollars a year for four years during the time that the recipient is actually enrolled in the Medical School of the University of Minnesota. The proposal is to grant one additional scholarship to a beginning medical school student each year until four have been awarded, so that the maximum cost of the scholarships will be four thousand ($4000) dollars the fourth year and each year thereafter."

### Stipulate Conditions

In order to assure that a doctor will be provided for a rural area in the state, the plan sets up certain conditions which must be agreed upon by the scholarship recipient: "The recipient, as a condition to being awarded the scholarship, must agree, at that time, that upon the successful completion of his medical education, including an internship of not exceeding two years and licensure in the State of Minnesota, to engage full time in general practice in a town of 5,000 population, or less, for a period of not less than five years. Failure upon the part of the recipient of the scholarship to do so, will make it necessary for the student to return to the scholarship fund of the Minnesota State Medical Association, the same percentage of the total grant as is represented by the uncompleted portion of the five-year period, together with interest thereon at a modest rate. For example, if the doctor serves only two years of the five-year period, he must return three-fifths of the total amount awarded him from the scholarship fund. Upon the completion of the five-year period the doctor is discharged from any indebtedness to the fund."

### Plan of Selection Outlined

Certain basic requirements for the selection of medical students to receive the grant were outlined for the House by the committee. Responsibility for selection is vested in the Rural Medical Scholarship Selection committee, with advice and assistance from the University Relations committee, the Dean of the Medical School and members of the Council and such others as may be called upon by the committee. The report states:

"(3) Among the basic requirements that will serve as a guide for this committee in awarding such scholarships will be:

(a) The character of the individual.

(b) The true desire of such person to study medicine and to become a practitioner of medicine.

(c) Residence in a rural area or a town of less than 5,000 population, in Minnesota.

(d) Willingness of student to engage in general practice for not less than five years in a town of the student's selection; the selection, however, to be made from a list to be prepared by this committee after consultation with various interested groups and individuals as the committee may determine or be directed by the Council."

### Good Results Anticipated

It is hoped that final details of the plan can be completed so the committee can choose the first recipient of the scholarship for the fall quarter of 1952. The committee report emphasized that "while the plan partakes of the nature of a loan, it is an outright grant of the award to the recipient when the recipient has complied with his part of the agreement."

In avoiding hazards encountered by other states in granting scholarship awards, the committee felt that the ultimate good to be realized far outshines

the somewhat cautious start the plan is undergoing. The long-range results are stated by the committee thusly: "Unlimited good to everyone concerned, including the public generally, recipients of the scholarship, and the medical profession, can result from this project."

## AMA PRESIDENT LAUDS HIGH STANDARDS

Praising the American Medical Association's long fight to establish high medical standards and constantly to improve upon them, Dr. Louis H. Bauer, new president of the AMA, paid tribute to those efforts with these words in his inaugural address: "During the entire history of the American Medical Association, with just one exception, there has been no major Federal health law enacted that was not either sponsored or supported by the Association."

Dr. Bauer outlined a brief history of the association's efforts, through its committees and councils, for attainment of high standards for foods, nutrition, cosmetics, apparatus and industrial health, and other scientific areas.

In the field of medical education Dr. Bauer said, "The Association first came under heavy fire nearly a half century ago, when it began its campaign to raise the standards of medical education in this country. Medical education was at a low ebb, and it was imperative that the low grade medical schools and diploma mills existing at that time be eliminated. The campaign was successful and today we have only high grade schools of medicine in the United States. One dramatic proof of this campaign's success lies in the fact that today this country is the Mecca for medical training. Nowhere in the world is the level of medical education higher. Nowhere in the world is there a higher standard of medical care."

Stating that the AMA has more recently been equally vigilant in developments in the socio-economic fields related to medicine, Dr. Bauer felt that critics had been unjust in denying the Association's right to strive for improvements in that field as well:

"Now, the association is told that its scientific activities are all right, but its socio-economic policies are all wrong. Twenty years ago we were criticized because we dared to question some of the developing health insurance plans. What was overlooked, of course, was the fact that no criteria had been established at that time by which to assess such insurance, and that little reliable information about it was then available. A year later we recommended experimentation in that field, and listed safeguards to be included in plans for the protection of patients. As a result, Voluntary Health Insurance has become the fastest growing insurance project in history, and is providing a sound means for prepayment of the major costs of illness. Yet, now we are vilified because we do support it and because we continue to oppose Compulsory Health Insurance."

### Promises Continuing Efforts

As the association's leader for the coming year, Dr. Bauer pledged the medical profession to continuing efforts to raise medical and health standards for America. He stated that it is not enough that America has the world's highest standards of medical care, but that this type of service must reach the entire population. He urged expansion of public health facilities, and co-operation from all concerned to solve any problems, so that large numbers of people shall not be without proper environmental sanitation, protection against communicable disease and protection of their food, milk and water supplies. He urged physicians to work for forward-looking plans for the care of chronic invalids and programs for the medical care of the indigent. He noted that studies of medical care are constantly in progress:

"Studies of the various methods of delivering medical care are being carried on by the American Medical Association, and these studies will be continued. It becomes increasingly apparent that no one method provides the answer for every area and every group of citizens. That is one of the medical profession's objections to any government-controlled type of medical care plan. Under such a plan the same system would be imposed on every region and every individual regardless of need or local conditions."

## WISCONSIN EDUCATOR ADDRESSES STATE MEETING

"One of the disturbing aspects of the contemporary scene is the fact that in steadily pushing frontiers in the field of science ahead at an accelerated pace, we have widened the gap between technological achievement and man's adjustment to that achievement."

That theme was presented by Dr. J. Martin Klotsche, president of Wisconsin State College in Madison. Dr. Klotsche spoke at the annual banquet of the Minnesota State Medical Association on May 27.

Dr. Klotsche said that Americans cannot record

*(Continued on Page 704)*

# ✦ Reports and Announcements ✦

## AMERICAN COLLEGE OF SURGEONS

The thirty-eighth annual Clinical Congress of the American College of Surgeons will be held at the Waldorf-Astoria in New York City from September 22 to 26, 1952.

Surgeons from all parts of the nation and a number of foreign countries will assemble to take advantage of the program which will include clinics, postgraduate courses, forums, panel discussions, color television and scientific and technical exhibits. Some sixty-two hospitals in the New York area will participate in the program of operative clinics and demonstrations.

At the presidential meeting, September 22, Dr. Alton Oschner of New Orleans will give the presidential address; Dr. Donald C. Balfour, Rochester, Minnesota, will give the seventh Martin Memorial Lecture on "The Evolution of Gastric Surgery" and Dr. Harold Foss, Danville, Pennsylvania, will be installed as president for 1953. At the convocation, September 26, Sir Cecil Wakeley of London, president of the Royal College of Surgeons, England, will give the Fellowship address.

Headquarters of the College are at 40 East Erie Street, Chicago.

## MINNESOTA VALLEY GENERAL PRACTITIONERS AND RENVILLE COUNTY SOCIETY HOLD JOINT MEETING

At a joint meeting of the Minnesota Valley chapter of the American Association of General Practitioners held in Renville in May, the need for more trained nurses and the importance of the general practitioner in small communities were the main points of discussion.

Dr. Willis L. Herbert, general practitioner at St. Mary's Hospital, Minneapolis, was the feature speaker of the meeting. He gave the keynote of the meeting in stating that the AAGP is doing much to keep general practitioners from being replaced by specialists.

Dr. James Cosgriff, Sr., president of the AAGP unit and a member of the State Board of the AAGP, said "The public deserves a general practitioner" in defense of the country doctor as opposed to the specialists in metropolitan areas.

At the business session, Dr. W. E. Hines of Willmar was elected to succeed Dr. Cosgriff as president. Elected as secretary was Dr. James Cosgriff, Jr. of Olivia.

## CONTINUATION COURSE IN ROENTGENOLOGY

The University of Minnesota will present a continuation course in *Gastro-Intestinal Roentgenology for Radiologists* from October 20 to 25, 1952. The course will be presented at the Center for Continuation Study on the University campus and will cover all aspects of roentgenologic examination of the gastro-intestinal tract.

The distinguished visiting faculty members will include: Dr. Olle Olsson, Professor, Department of Diagnostic Roentgenology, University of Lund, Lund, Sweden; Dr. Richard R. Schatzki, Chief, Department of Roentgenology, Mt. Auburn Hospital, Cambridge, Massachusetts; Dr. Frederic E. Templeton, Professor, Department of Radiology, University of Washington Medical School, Seattle; Dr. Paul C. Swenson, Professor, Department of Radiology, Jefferson Medical School, Philadelphia, Pennsylvania, and Dr. Leon Schiff, Associate Professor, Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio.

On Wednesday, October 22, the Annual Leo G. Rigler Lecture will be presented by Dr. B. J. Kirklin, Professor, Department of Radiology, Mayo Foundation, Rochester.

The course will be presented under the direction of Dr. Leo G. Rigler, Professor and Head, Department of Radiology and Physical Medicine, and the remainder of the faculty will include members of the clinical and full-time faculty of the University of Minnesota Medical School and the Mayo Foundation.

## LYON-LINCOLN COUNTY SOCIETY

Members of the Lyon-Lincoln County Medical Society entertained the attorneys of the two counties at a dinner in Chuck's cafe, Hendricks, on June 2. Speaker of the evening was a Minneapolis attorney, R. A. Scallen, who gave a very informative talk on "The Doctor in Court." Thirty-five members and guests were present. This has become an annual occasion among the legal and medical men of these two counties over the past few years.

## SAINT LOUIS COUNTY SOCIETY

The second annual press conference of the Saint Louis County Medical Society was held May 23 in St. Luke's Hospital, Duluth. Duluth and Iron Range newspaper representatives were in attendance.

Sessions started with a panel of medical men and hospital administrators, Dr. Martin O. Wallace acting as moderator. Richard Fox, assistant administrator of St. Luke's and Sister Loretta, St. Mary's Hospital administrator, discussed "Facts about Hospital Costs." Dr. Earl Barrett, Duluth pediatrician, spoke on "Modern Methods for Salvage of Premature Infants." A motion picture entitled "The Romance of Aureomycin" was shown by Harry Haney.

The conference ended with a banquet in the Kitchi Gammi Club. Principal speaker was Dr. William P. Shepard, San Francisco, vice president of the Metropolitan Life Insurance Company. His subject was "Public Health and Socialized Medicine." Dr. L. R. Gowan was banquet toastmaster.

Honored at the banquet was Dr. Albert J. Chesley of Saint Paul, director of the Minnesota Department of Health, who has completed fifty years of service in the medical field.

*(Continued on Page 684)*

## SOUTHERN MINNESOTA MEDICAL ASSOCIATION

The annual meeting of the Southern Minnesota Medical Association will be held at Austin on Monday, September 8.

The following program will be presented:

### Program

*Morning Session*

1. "Migraine: Diagnosis and Treatment"
   GUSTAVUS A. PETERS—Rochester
2. "Physical Symptoms of Depression"
   WILLIAM S. CHALGRIN—Mankato
3. "Use of Compound F in the Treatment of Post-traumatic Bursitis of the Knee and Ankle"
   E. D. HENDERSON—Rochester
4. "Treatment of Cutaneous Malignancies"
   L. M. HAMMAR—Mankato
5. "Urgent Surgical Conditions in New Born Period"
   A. B. HAYLES—Rochester
6. "Problems of Diseases of the Thyroid other than Hyperthyroidism"
   MARTIN A. NORDLAND—Minneapolis
7. "Melanin Spots of the Lips, Buccal Mucosa, and Digits with Associated Intestinal Polyposis"
   LLOYD F. SHERMAN—Minneapolis
8. "Management of Cases with Leakage from Duodenal Stump after Partial Gastrectomy"
   C. E. REA—St. Paul
9. "The Responsibility of the Practising Physician and Health Department in the Case of the Aged"
   ROBERT N. BARR—Minneapolis

*Afternoon Session*

10. "Freedlander's Pneumonia—Case Report"
    JOHN P. DAHLSTET—Mankato
11. "Dissecting Aneurysm: Physical and Autopsy Findings—Case Report"
    EDWIN J. BENJAMIN—Minneapolis
12. "Methods of Internal Fixation in Operative Treatment of Fractures of the Hip and Shaft of the Femur—Case Report"
    HAROLD J. ANDERSON—Austin
13. "Danger of Use of Cortisone in Acute Rheumatic Fever and Concurrent Renal Damage"
    C. H. SCHEIFLEY—Rochester
14. "Perforation of Rectum with Unusual Complications—Case Report"
    W. C. BERNSTEIN—St. Paul
15. "Coronary Insufficiency"
    BURTIS J. MEARS—St. Paul
16. "Doctors' Disagreements in Court"
    JOSEPH C. MICHAEL—Minneapolis
17. "Neurosurgical Treatment of Intractable Pain Due to Metastatic Carcinoma"
    H. J. SVIEN—Rochester

## NORTHERN MINNESOTA MEDICAL ASSOCIATION

The Northern Minnesota Medical Association will hold its annual meeting at Crookston, Minnesota, Friday and Saturday, August 22 and 23. Officers of the association are: Dr. George Sather of Fosston, president; Dr. W. S. Neff of Virginia, vice president; and Dr. C. L. Oppegaard, of Crookston, secretary-treasurer.

The scientific program to be presented is as follows:

### Friday, August 22

A.M. *Morning Session*

9:00 "Diagnosis of Subdural Hematoma, Particularly in Children"
GORDON J. STREWLER, M.D., Duluth

9:45 Discussion Period

10:00 "Psychiatric Treatment for the Neurotic Patient"
JOHN E. T. HAAVIK, M.D., Duluth

10:45 Discussion Period

11:00 "The Management of Endometriosis"
JOHN E. FABER, M.D., The Mayo Clinic, Rochester

12:00 Business meeting

P.M. *Afternoon Session*

2:00 "Certain Aspects of Biliary Tract Surgery"
RICHARD L. VARCO, M.D., University of Minnesota, Minneapolis

2:45 Discussion Period.

3:00 "The Insurance Aspects of Heart Disease"
HARRY E. UNGERLEIDER, M.D., Director of Medical Research, Equitable Life Assurance Society, New York, N. Y.

3:45 Discussion Period.

4:00 "Prevention and Treatment of Respiratory Tract Infections."
HOBART A. REIMAN, M.D., Philadelphia, Pa.

*Evening Program*

7:00 Annual Banquet
Address: "An American Looks at Asia"
MORRIS WEE, D.D., First Lutheran Church, Duluth

### Saturday, August 23

*Morning Session—9:00-12:00 Noon*

Clinico-Roentgenological-Pathological Conference
Conducted by HENRY MOEHRING, M.D., of Duluth and associates.

A full program of entertainment has also been planned for members of the Ladies' Auxiliary.

*To open congested air passages in hay fever*

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***. . . reduces nasal engorgement . . . relieves soreness***

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The resultant relief to the hay fever sufferer is decidedly gratifying. Prolonged action of Neo-Synephrine makes fewer applications necessary, consequently longer periods of rest and sleep are possible.

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1. Van Alyea, O. E., and Donnelly, Allen: *Arch. Otolaryng.*, 49:234, Feb., 1949.

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# Woman's Auxiliary

## RAMSEY AUXILIARY AIDS REHABILITATION CENTER

The Woman's Auxiliary to the Ramsey County Medical Society has contributed a whirlpool bath to the newly enlarged Saint Paul Rehabilitation Center, which has moved to the Wilder Health Center. The new whirlpool bath will be used in the therapeutic nursery.

In accepting the gift on behalf of the Rehabilitation Center, Mr. Louis S. Headley, president, expressed his appreciation and thanks and stated: "This gift by the Auxiliary will be part of the center's permanent equipment and will provide treatment for hundreds of children throughout the years. The Auxiliary is to be congratulated for selecting this most useful gift as its community project for the years 1952-53."

The whirlpool bath will be used to provide hydrotherapy for children. The whirlpool provides a combination of heat and massage through the agitation by air of thermostatically controlled water. Its use is of particular advantage in the treatment of strains and sprains, in the rehabilitation of fractures where active and passive motion, along with heat and massage are desired, and in the treatment of other conditions where relaxation of muscles is essential.

### Center Notes History

In moving into enlarged quarters, it was noted that since the opening of the center in 1948, the center has treated approximately 2,300 patients, with referrals by 330 doctors.

The Saint Paul Rehabilitation Center was originally opened in 1948 on the fourth floor of the Wilder Dispensary building on Rice street. It was sponsored and financed by the Minnesota Society for Crippled Children and Adults, the Saint Paul Junior league, and the Wilder charity to make available to the people of Saint Paul and its environs the services of physical, occupational and speech therapists upon the referral of a physician. The original staff consisted of the director, who was also the speech therapist, a physical therapist, an occupational therapist, and an office secretary.

During the first year 100 doctors referred 366 patients, who made 7,222 visits to the center.

By the end of the first year it was evident that the approximately 2,800 feet available to the center in the Wilder Dispensary Building was entirely inadequate. Although the staff had been tripled in size, the space available was not adequate for proper treatment of the patient load. The center served an approximate average of 670 patients during both the second and third years.

For the first three years the Rehabilitation Center was operated as a voluntary nonprofit association and was governed by an Executive committee made up of representatives of the three sponsors and the Family Nursing Service. In the summer of 1951 the Saint Paul Rehabilitation Center was incorporated with a representative Board of Directors of twenty-five, nine of whom represent the three sponsors.

### Advisory Group Appointed

Before undertaking to establish the center, the original sponsoring committee, which was appointed by the Board of Directors of Family Nursing Service, obtained the approval of the Ramsey County Medical society and the endorsement and support of a number of leading physicians. From the beginning, the center has had the benefit of the advice and counsel of a medical advisory committee, which at present is made up of Dr. Frank Adair, Dr. John J. Beer, Dr. Carl C. Chatterton, Dr. Harold F. Flanagan, Dr. Ernest M. Hammes, Dr. Albert F. Hayes, Dr. Alfred J. Ouelette and Dr. Hyman Lippman. The medical advisory committee acts as a liaison with the medical profession and recommends to the governing board all medical policies.

The new center is planned so that the various phases of treatment can be co-ordinated to provide the patient the greatest possible assistance toward resuming his place in the community.

In addition to the whirlpool bath contributed by the Ramsey Auxiliary, the center has three such whirlpool baths as well as a large Hubbard tank in the hydrotherapy section of the physical therapy department. The center also has a lamp room with individual treatment booths and a gymnasium.

Craft and activities for daily living will be taught in the occupational therapy department. A new kiln has been installed for the ceramics unit, and a print shop and looms have been set up in separate rooms.

The speech therapy department will have nine treatment rooms, two supplied with facilities for testing, hearing and special audio-amplifying and sound recording equipment. Two others have one-way windows for observation, important in speech training.

The remodeled Wilder Public Bath building, undertaken by the Board of Directors of the Wilder Charity, and now known as the Wilder Health Center, is owned and operated as a community service by the Wilder Charity. The entire cost of remodeling was paid by this charity and space occupied by the Rehabilitation Center and Family Nursing Service is provided rent-free. The remodeling was completed about June 1 and shortly after the Rehabilitation Center moved into its enlarged quarters which were planned and designed to meet its special medical requirements. In its new quarters it is believed to be one of the finest and most complete rehabilitation centers in this area.

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It will be easier to obtain the support needed for an effective health program if it can be shown that such a program will not only enrich the individual human life but will also bring to the community which invests in health tangible economic benefits. Prevention is not only better than cure; it is also cheaper than cure. C. E. A. Winslow, "The Cost of Sickness and the Price of Health," *W.H.O. Monograph Series*, No. 7, 1951.

# In Memoriam

## CHARLES DONEY FREEMAN

American dermatology lost an outstanding representative and all who knew him a loyal friend when Charles D. Freeman died on April 18, 1952.

Dr. Freeman was born in Saint Paul on January 25, 1879. He was graduated in Medicine from the University of Minnesota in the class of 1904 and served his internship in the Saint Paul Lutheran Hospital. In the company of Dr. Egil Boeckmann he then went abroad where he studied under the great dermatologic masters in Europe for two years, especially those of Vienna, Paris and London. Much of the time was spent with the eminent teacher, Max Joseph of Berlin. Returning to Saint Paul he practiced his specialty until his terminal illness began.

As an assistant professor of dermatology of the University of Minnesota, he was a diligent teacher at Ancker Hospital and the Saint Paul Dispensary.

Dr. Freeman was a member of the American, Chicago and Minnesota Dermatological societies and the first president of the latter. He was a constant attendant of the Minnesota Academy of Medicine and its president in 1933. He was a member of the Ramsey County Medical Society, the Minnesota State Medical Association, the American Medical Association and the Clinical Club of Saint Paul. He was attending dermatologist at the Charles T. Miller, St. Joseph's and St. Luke's hospitals. He originated the treatment of Kerion Celsi with solid carbon dioxide.

Dr. Freeman served as a captain in World War I.

Although he was a distinguished physician in every sense of the word, it was as an individual that he attained great esteem in the eyes of his friends. Rarely could one find a man who adhered so strictly to a rigid code of conduct. He staunchly defended his principles and friends and as vehemently condemned what he considered sham or unethical practices. He was abrupt, concise and at times caustic in his manner of speech, but was ever ready to be corrected if shown to be misinformed. He loved life and thoroughly enjoyed to sit around the festive board with his friends, who came from all walks of life. A man, if proven, was a man with Charlie and he never inquired about his origin, creed or color. He greatly enjoyed fishing, hunting and bridge and had particular companions for each.

Dr. Freeman married Caroline Boeckmann on January 1, 1910, the daughter of his greatly respected guide and teacher Dr. Edward Boeckmann and their marriage was an ideal example of devotion, understanding and mutual admiration. He is survived by his widow, a son, and two daughters: Dr. Charles D. Jr., Caroline M. (Mrs. W. D. McCall), and Helga B. He also has two grandchildren, Willard D. McCall, Jr., and Charles Freeman McCall, All live in Saint Paul.

The friendship of Charlie Freeman and the late Dr. John Butler was one of those rare companionships that became a legend. They attended all medical meetings together, they were close social friends, and they complemented each other in so many ways that they could never be thought of but jointly. Even though they had contrasting personalities, their attraction for each other began in medical school and continued unabated throughout their lives. Charlie thought of Doctor Henry Michelson of Minneapolis as his special protegé and their association was very close.

Dr. Freeman considered life an adventure which was to be experienced without regret or protest. He accepted the good with the bad and believed wholeheartedly in the supremacy of the individual. He neither sought nor would accept patronage and the mere mention of a socialized order of society brought forth his most vigorous protest.

One of the most gratifying and proud moments in Doctor Freeman's life was to see his son assume his dermatological practice in Saint Paul and, as Charlie put it "do well."

He was a grand man with many unique and lovable qualities and he will be long remembered by his many friends whose deep sympathy is extended to his surviving family.

JOHN F. MADDEN, M.D.

## WILLIAM FRIESLEBEN

Dr. William Friesleben of Sauk Rapids, Minnesota, died May 20, 1952, at the age of seventy-four.

Dr. Friesleben was born in Livingston County, Illinois, February 10, 1878. He obtained a B.S. degree from Valpariso, Indiana, in 1901 and an M.D. degree from the Ohio Medical College at Cincinnati in 1906. In 1907 he moved to Sauk Rapids, where he practiced continuously for the past forty-five years.

On June 30, 1946, his many friends set the day aside as Friesleben Day and paid tribute to the doctor in recognition of his long and faithful service to the community. Over 2,500 persons attended the celebration.

Besides practicing, Dr. Friesleben served many years on the Public School Board, the Benton County Fair Board, the Village Board of Health and as County Coroner. He was a past chief-of-staff of the St. Cloud Hospital and past president of the Stearns-Benton County Medical Society. He was a member of the Minnesota State Medical Association and the American Medical Association.

Dr. Friesleben is survived by his wife; a brother, Arthur, and a sister, Mrs. Emma Wunch, both of Pontiac, Michigan.

## WILLIAM A. KENNEDY

Dr. William A. Kennedy, Saint Paul, died on April 30, 1952, following a long illness.

Dr. Kennedy was born August 1, 1893, in Minneapolis. He obtained his medical degree from the University of Minnesota in 1918 and took postgraduate work in the

*(Continued on Page 704)*

# Of General Interest

**Dr. Neil S. Dungay,** one of the best known and best loved professors at Carleton College, Northfield, was officially retired from the faculty as of Monday, June 30, this year.

Dr. Dungay, professor of hygiene and public health, came to Carleton in 1907. He received his B.A., M.B. and M.D. degrees from the University of Minnesota; his Ph.D. from the University of Chicago. A member of Phi Beta Kappa and of Sigma Xi, Dr. Dungay is also a member of Alpha Omega Alpha, honorary medical society, Phi Beta Pi, medical fraternity, and a Fellow of the American Association for the Advancement of Science.

He is a member of the American Medical Association, Minnesota State Medical Association and of the Rice County Medical Society. He has served as president of the North Central Section of the American Student Health Association. Dr. Dungay esablished the first organized Carleton College Health Service in 1925 and was a physician in the Health Service and its director for many years. For many years, Dr. Dungay has been a member of the Woods Hole Corporation, Cape Cod Marine Biological Laboratory.

An interesting fact in Dr. Dungay's career at Carleton is that Dean Horace Goodhue, who came to Carleton in 1867, was still at the College at the time of Dr. Dungay's appointment in 1907, thus making Dr. Dungay's and Professor Goodhue's years of service at Carleton cover the entire history of the college.

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**Dr. Olin West,** for twenty-three years secretary and general manager of the American Medical Association, passed away June 19 at his home in Nashville, Tennessee. Dr. West retired on April 1, 1946, and had been living in Nashville since that time.

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**The American Heart Association** announced that it has approved seventy-two grants-in-aid totaling $361,522.50 to research being conducted in twenty states, the District of Columbia, Montreal and Beirut, Lebanon. This increases to $578,172.50 the amount awarded under the National Association's research program during the fiscal year and raises to over four million dollars the total amount appropriated during the past four years.

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Beginning with the January 1953 issue, the *New Orleans Medical and Surgical Journal* will become the *Journal of the Louisiana State Medical Society.* The journal has had its present name since 1844 and is one of the oldest journals in the country. As it is now the property of the Louisiana State Medical Society, the new name properly attests that it represents the profession of the entire state and not simply that of New Orleans.

**Dr. Orville H. Jones,** Mankato, moved his office from 303 National Citizens Bank to 1008 South Front Street on May 15, 1952.

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**Dr. Karl A. Meyer,** president of the Cook County Graduate School of Medicine, has announced the receipt by the school of a donation of $100,000 from the Joseph and Helen Regenstein Foundation. Presentation of the donation was made on the occasion of the official opening of the school's new building located at 707 South Wood Street, Chicago, Illinois.

* * *

Among a total of seventy-four retiring professors and employes of the University to receive certificates from President Morrill upon their retirement from the faculty in June were: Dr. Walter C. Alvarez, Dr. Moses Barron, Dr. William L. Benedict, Dr. David M. Berkman, Dr. Willard L. Boyd, Dr. Harry H. Bowing, Dr. Albert C. Broders, Dr. Della G. Drips, Dr. Bert E. Hempstead, Dr. Norman M. Keith, Dr. Edward C. Kendall, Dr. Henry W. Meyerding, Dr. Robert D. Mussey, Dr. Gordon B. New, Dr. John de J. Pemberton, and Dr. Russell M. Wilder.

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**Notes from the AMA Meeting**

In his address to the House, Speaker Francis F. Borzell, Philadelphia, revealed that the average age of a member of the House is only 59 years and that the average length of service in the House is five and one-half years. . . . The Chicago Medical Society contributed $25,000, the Woman's Auxiliary to the AMA, $10,000, and the American College of Radiology, $2,000 to the American Medical Education Foundation. . . . To save time and cover more ground quickly, Bob Lyon of the AMA business and advertising department borrowed his young daughter's roller skates and used them to coast up and down the mile-long Navy Pier, home of the scientific and technical exhibits. . . . Dr. Herbert McLean Evans, Berkeley, Calif., was the recipient of the $5,000 Passano Foundation Award for 1952. . . . Boston heart specialist Paul Dudley White made a flying trip to Chicago to accept the AMA Distinguished Service Award for 1952. . . . Dr. Charles Donatelli, Toledo, won the 1952 championship of the American Medical Golfing Association with a 36-hole score of 154 (76-78).

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**Dr. W. McKraig,** Rochester, received an honorary degree from Ohio Wesleyan College.

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**Dr. Lyle Benson,** who was released from the Army recently, has returned to Tracy with his family from Camp Rucker, Alabama, where he had been serving as commander of the 104th Clearing Com-

*(Continued on Page 692)*

*(Continued from Page 690)*

pany of the 47th National Guard division. Dr. Benson resumed his medical practice with the Hoidale-Workman Clinic in Tracy on June 15.

* * *

**Dr. Louis A. Brunsting,** member of the section of dermatology of the Mayo Clinic, Rochester, and professor of dermatology and syphilology in the Mayo Foundation, left in June for a two and a half month trip in this country and Europe. Highlight of his trip will be attendance at the International Congress of Dermatology and Syphilology in London, July 21-26, as United States secretary of the Congress. He is chairman of a symposium on "Cortisone and Corticotropin (ACTH): Their Effects on the Skin and Its Diseases," and will present a paper on effects of these hormones in lupus erythematosus and other collagen diseases. He will also demonstrate an exhibit prepared in association with Drs. R. R. Kierland and P. A. O'Leary on "Cortisone and Corticotropin (ACTH): Their Use in Dermatology."

Dr. Brunsting will attend medical clinics in Edinburgh, Scotland, and on the continent. He will present papers at the Munich Dermatologic Society meeting July 5 and in Leyden, Holland, before the faculty of the University of Leyden, July 17. He will also give a clinic for medical students in Stockholm, Sweden. The Brunstings will return to Rochester, August 25.

**Dr. K. A. Danford,** who completed his service with the Naytahwaush Clinic, Mahnomen, in June, was honor guest at a farewell luncheon given by members of the various communities served by the Clinic, and was presented with a purse in appreciation of his "long and faithful" service. Dr. Danford, who has served as visiting physician for the Clinic during the past five years, will be succeeded by **Dr. Mildred Nordlund** of White Earth.

* * *

**Dr. H. De Boer** of Edgerton and **Dr. A. H. Brown** of Pipestone were awarded life memberships in the Southwestern Minnesota Medical Society at a recent meeting in Worthington. Dr. De Boer has been a practicing physician for more than forty years and Dr. Brown has practiced for more than fifty years.

* * *

**Dr. James H. DeWeerd,** member of the section of urology at the Mayo Clinic, Rochester, is now visiting medical centers in nine countries in Europe. Upon recommendation of the graduate committee of the Mayo Foundation, Dr. DeWeerd was named recipient of the Dr. J. William White award for foreign travel, which is given for superior achievement during fellowship in the Mayo Foundation and stipulates the completion of all requirements for an advanced degree of Master of Science in a surgical specialty. Dr. DeWeerd, accompanied by Mrs. DeWeerd, will visit medical centers in Paris, Rome, Berne, Zurich, Amsterdam, Copenhagen, Stockholm,

Oslo, Glasgow, Edinburgh, Newcastle-on-Tyne and London. The DeWeerds will return to this country in August.

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**Dr. L. M. Evans** of Sauk Rapids has received notification of his admittance to membership in the International College of Surgeons.

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**Dr. L. M. Ellertson** of Albert Lea was elected president of the Albert Lea Junior Chamber of Commerce at a meeting held late in May. Dr. Ellertson has practiced in Albert Lea with Drs. Erdahl and Nelson since September, 1950. He is a graduate of the State University of Iowa College of Medicine, and was a medical officer in the U. S. Navy and a resident physician at Ball Memorial Hospital, Muncie, Indiana, before coming to Albert Lea.

* * *

**Dr. Mario Fischer,** Duluth health director, has been elected a vice president of the National Tuberculosis Association. The election took place at the forty-eighth annual meeting held in Boston.

* * *

**Dr. Clare Gates,** director of health education in Minneapolis, resigned from the city health departmen, effective July 1, to become director of the health and medical care division of the Community Welfare Council of Hennepin County. He succeeds

Dr. M. B. Hesdorffer who resigned in June to become medical director of the Du Pont Company plant at Martinsville, Virginia.

* * *

**Dr. Lowell A. Gess** and his family were honor guests at a farewell reception early in June given by the Calvary Evangelical United Brethren Church, Saint Paul, on the occasion of their leaving for mission work in Nigeria, Britsh West Indes. Dr. Gess, who is a licensed minister in the United Brethren Church, is a graduate of Macalester College and received his M.D. degree from Washington University in 1951. He has been serving his internship at Ancker Hospital, Saint Paul.

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**Dr. R. I. Gruys** has terminated his practice at Windom, Minnesota, preparatory to early entry into the service, having received notice of his classification with selective service. He will visit friends and relatives in Chicago before going to his station.

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**Dr. Donald F. Holm,** who has been practicing in Wood Lake on a temporary basis, has announced that he will discontinue practice there effective July 1 in order to take care of his practice in Willmar. Before leaving Wood Lake, Dr. Holm addressed a meeting of the Farmers Union on the subject of "Mental Health." A motion picture on mental health was shown preceding Dr. Holm's talk.

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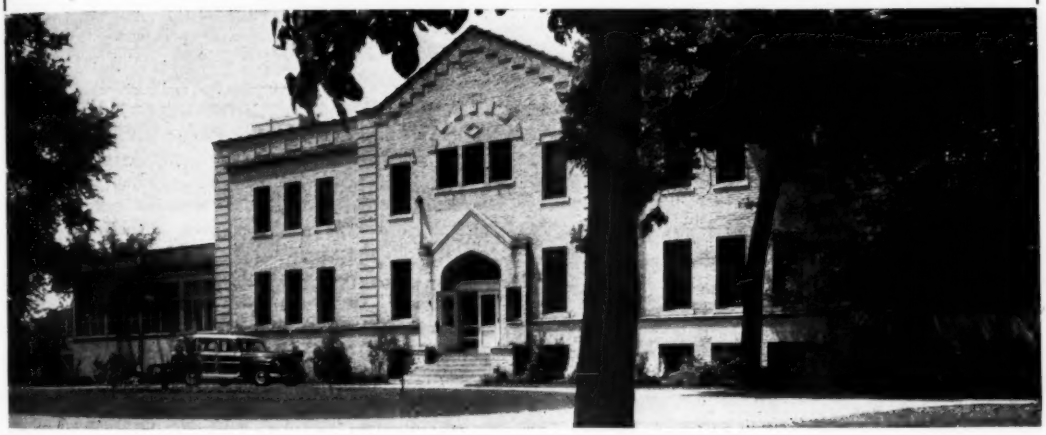
**Dr. Henry F. Helmholz,** chief of pediatrics at the Mayo Clinic, Rochester, is chairman of the National PTA Congress standing committee on health. He is one of nineteen new chairmen named at the group's fifty-sixth annual meeting in Indianapolis, Indiana. All will serve three years as committee chairmen and members of the PTA board of managers. Dr. Helmholz is emeritus professor of pediatrics at the University of Minnesota.

* * *

**Dr. John W. James,** son of **Dr. and Mrs. William H. James,** of Lake Crystal, and Miss Virginia Ann Winkle of Rochester were united in marriage, June 7, at a wedding ceremony held in Trinity Lutheran church, Rochester. Dr. and Mrs. James left for a wedding trip to California and have now returned



to Rochester where they will make their home. The bride is a graduate of the University of Minnesota school of medical technology and the University of Minnesota graduate school. Dr. James is a graduate of the University of Minnesota medical school.

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**Dr. M. E. Janssen,** Crookston, was guest speaker at a meeting of the Crookston chapter of Registered Nurses late in May, talked on the administration of the new drugs and cited the nurse's responsibility with regard to intravenous therapy. Dr. Janssen is a member of the Northwestern Clinic staff.

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**Dr. E. B. Kinports** of International Falls left in June for San Diego, California, where he will take three years of advanced medical work at Mercy Hospital. The hospital, a 350-bed institution, is operated by the Sisters of Mercy and is considered the largest in San Diego. Dr. Kinports plans to resume practice in International Falls upon completion of his study in San Diego.

* * *

The first comprehensive survey of rehabilitation facilities providing direct services for the physically handicapped was reported in June to the quarterly meeting of the Community Chest and Council of Hennepin County, Inc., by **Dr. Frank H. Krusen,** head of the Mayo Clinic section on physical medicine and rehabilitation, who directed the survey in Minneapolis and Hennepin County.

Dr. Krusen stated in his report that Minnesota has not been among the leaders in providing rehabilitation for the seriously disabled. It stands ninth from the bottom. Said Dr. Krusen, "It may be as humane to save one who is disabled from years of dependency as to save his life."

Recommendations made in the report are:

*Commendation* of the University of Minnesota for its establishment and planning for the division of physical medicine and rehabilitation, for training physicians and auxiliary personnel and the supervision of the rehabilitation program in University Hospitals and its affiliated institutions.

*Review* by the sponsoring committee, or another one specially constituted, of the information reported with the object of co-ordinating all existing facilities in rehabilitation and with the hope of eventually adding a rehabilitation center to these facilities.

*Assumption* of professional responsibilities for physical medicine and rehabilitation services at the Minneapolis Curative Workshop by the University of Minnesota physical medicine and rehabilitation division.

*Increased* budget and staff for the Minnesota division of vocational rehabilitation in the state department of education.

*Special Study* of problems of sheltered and homebound employment in Minneapolis and Hennepin county, with particular consideration of plans for expanding sheltered workshop facilities.

*Establish* a general registration of all handicapped persons.

*Expand* social service facilities in conjunction with rehabilitation programs.

Dr. Krusen emphasized that the first step to be taken locally should be co-ordination of existing facilities

with no intent to supersede the various agencies with a rehabilitation center.

He explained there is an immediate need for transfer and interchange of services between the existing agencies.

The ten critical services for rehabilitation work include registration, medical diagnosis, vocational diagnosis and guidance, rehabilitation planning, social welfare, treatment, training, selective placement, recreation and follow-up.

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**Dr. J. Grafton Love,** Rochester, received an honorary Doctor of Science degree from his alma mater, Wake Forest College, Wake Forest, North Carolina, during commencement exercises in June. He is a 1925 graduate of the college.

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**Dr. Charles W. Mayo** of the Mayo Clinic, Rochester, was re-elected to the Board of Directors of Northwest Airlines at the annual meeting of shareholders this year. Dr. Mayo, who has been active in aviation medical research and has served in the medical reserve corps, has been a member of the Airline's Board since 1948.

* * *

**Dr. Henry W. Meyerding** of Rochester was made an honorary citizen of the city of Bordeaux, France, recently, according to an announcement issued by the International College of Surgeons. Dr. Meyerding, who is president of the United States chapter of the college, together with Dr. Max Thorek of Chicago, founder and secretary-general of the college, were made honorary citizens of the French city during meetings of the French chapter, preliminary to the biennial international meeting at Madrid, Spain, in May.

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**Dr. Chris Melde** of Olivia has been chosen chairman of the Renville County chest x-ray survey to be conducted in all parts of the county between September 1 and November 15, this year.

* * *

**Dr. and Mrs. M. S. Nelson** of Granite Falls were honor guests at a reception and banquet given by members of the local hospital board in recognition of their long activity in hospital work in the community. In commemoration of the event, Dr. and Mrs. Nelson were presented with a bronze plaque.

* * *

**Dr. Siegfried Oeljen** of Waseca was speaker of the evening at a recent meeting of 4-H Club leaders of Waseca County. He discussed proper use of the eyes with regard to conservation of sight and gave an illustrated talk on proper posture and correct reading distance. In doing this, he also illustrated the reasons for many eye difficulties.

* * *

Newest member of the medical staff at Community Health Center, Two Harbors, is **Dr. Robert H. Painter,** native of Starkesboro, Vermont. Dr. Painter is a graduate of Jefferson Medical College in Philadelphia and served his internship at the Edward J.

*(Continued on Page 698)*

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Meyer Memorial Hospital, Buffalo, New York. Dr. Painter practiced at Collbran, Colorado, prior to coming to Two Harbors.

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**Dr. D. R. Philp** of Windom is now associated in practice with Dr. L. J. Hoyer as a partner in the Windom Clinic. The partnership was formed following two years of association in private practice.

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**Dr. E. N. Peterson** of the Lenont-Peterson Clinic, Virginia, was a speaker on the program of the Lake Superior Mines Safety Council held in Duluth late in May. His subject was "Medical Programs in the Mining Industry."

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**Dr. and Mrs. D. E. Pohl** and their two sons left Crookston in May for Boston, where Dr. Pohl is taking a three months' course in Boston City Hospital. Upon completion of the course, sponsored by Harvard University, Dr. Pohl will move his family to Austin, Texas, where he will resume medical practice about September 1.

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**Dr. John Pone,** who has just completed his intern training at Deaconess Hospital, Minneapolis, will become associated with the Osseo Clinic, Osseo, this month. Dr. Pone was born in Riga, Latvia, is a graduate of the University of Latvia and later became a specialist in surgery. He brings a wealth of medical and surgical experience to the community in which he will practice as he owned a private hospital in his native country, was surgeon at the Municipal Hospital of Libau and later worked in the same capacity in a hospital in Germany. He has done much in the field of reconstructive surgery and is the author of a number of books on various medical subjects.

* * *

**Dr. Edward H. Rynearson** of Rochester received an honorary Doctor of Science degree from his alma mater, Ohio Wesleyan University, at commencement time in June. Dr. Rynearson was graduated from Ohio Wesleyan in 1922.

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**Dr. Sheldon C. Reed,** of the Dight Institute of Human Genetics, University of Minnesota, was principal speaker on "The Biology of Mental Deficiency" at the concluding meeting of the Minnesota Society for the Mentally Retarded held in Saint Paul in June.

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**Dr. R. B. Skogerboe** of Karlstad gave the Memorial Day address in Newfolden at the special program given under the auspices of the Otto Knutson Legion Post and Auxiliary, May 30.

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Following completion of a postgraduate course in surgery in Philadelphia, **Dr. Peter J. Schultz** has returned to his practice in Minneapolis. En route home, Dr. and Mrs. Schultz visited the New England states, Canada and Niagara Falls.

**Dr. and Mrs. W. E. Richardson** of Saint Paul were honored at an open house in observance of their Golden Wedding anniversary in June. Dr. Richardson, a graduate of Rush Medical College in 1896, spent most of fifty years in practice in Slayton, Pipestone, and Rushford. After retiring from general practice in 1948, he served as plant physician in Morrels' Packing Plant at Sioux Falls, South Dakota.

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**Dr. Edward L. Tuohy** of Duluth discussed "Feeding the Aged and Chronically Ill" before the eleventh annual institute of Friends of the Land, July 1, at the University of Illinois medical center in Chicago. The institute is addressed each year by scientists, health workers, soil experts, farmers and nutritionists with emphasis placed on food and soil developments.

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**Dr. L. A. Vadheim** of Tyler, physician and surgeon in Lincoln County for more than forty years, presented a paper on "Control of Tuberculosis in Lincoln County" at the annual convention of the American Medical Association in Chicago in June. Lincoln County was the first county in the world to be accredited tuberculosis-free and the first to hold a survey and x-ray chest examinations of all persons in the county.

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**Dr. Kathlene Jordan** of Riverside Sanatorium will visit county schools in Lyon County the latter part of September and early October for a county-wide tuberculin-testing survey. Adults as well as school children will be included in the survey, according to Dr. W. H. Valentine of Tracy, president of the County Tuberculosis and Health Association.

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**Dr. and Mrs. S. W. Watson** of Royalton attended the meeting of the American Medical Association in Chicago in June.

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While attending the annual convention of the American Medical Association in Chicago in June, **Dr. and Mrs. Harold Wahlquist** of Minneapolis celebrated their twenty-eighth wedding anniversary. They contributed $100.00 to the American Medical Education Foundation fund as a wedding anniversary gift. Mrs. Wahlquist is the immediate past president of the Woman's Auxiliary to the American Medical Association.

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**Dr. E. P. K. Fenger,** staff member of Glen Lake Sanatorium, Oak Terrace, has been elected to the Board of the Hennepin County Tuberculosis Association. Dr. Asher White of Minneapolis was re-elected president.

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**Dr. and Mrs. H. H. Young** of Rochester attended a combined meeting of the American and British Orthopedic Associations in London, England, in June.

## HOSPITAL NEWS

At the annual meeting of the medical staff of St. Lucas Deaconess Hospital of Faribault, held in Kenyon at the home of the retiring president, Dr. R. R. Moses, on June 3, the following officers were elected for the ensuing year: Dr. Donald J. Studer, Faribault, president; Dr. F. C. Meyer, Kenyon, vice president; Dr. B. A. Orr, Faribault, secretary.

Dr. Robert Kierland, dermatologist at the Mayo Clinic, Rochester, presented a paper on "Common Skin Diseases" following the business meeting.

Members of the staff were entertained at dinner by Dr. and Mrs. R. R. Moses.

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Dr. John O'Leary was elected chief of staff of Northwestern Hospital, Thief River Falls, at a meeting of the staff held in May. Dr. J. Biedermann was elected vice chairman, and Dr. Paul Wendt, secretary-treasurer.

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Dedication ceremonies and open house were held in the new $750,000 addition to Fairview Hospital, Minneapolis, Sunday, May 25. Dr. J. A. Aasgaard, president of the Evangelical Lutheran church, gave the dedicatory address.

Guided tours through the new addition followed the program of speakers and musical numbers. The new building in the rear of Fairview Hospital contains surgical rooms, class rooms, a dining room, kitchen, laundry and storage facilities.

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Dr. Edmund B. Flink, formerly of Cambridge, has been appointed chief of medical service of the Minneapolis Veterans Administration Hospital. He will retain affiliation with the University of Minnesota as associate professor of medicine.

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Dr. John Reitmann, superintendent of the Sandstone State Hospital, has resigned and will continue his psychiatric training at Rochester State Hospital, as soon as a successor is named to fill his place at Sandstone.

## BLUE CROSS-BLUE SHIELD

*Minnesota Blue Shield Benefits Exceed $1,000,000 in 1952.*—Over $1,237,927 in Blue Shield benefits were received by Minnesota subscribers during the first four months of this year, Arthur M. Calvin, executive director, reported after the fifth annual board meeting of Minnesota Medical Service, Inc. (the Blue Shield Plan), held in conjunction with the Minnesota State Medical Association's ninety-ninth annual meeting, May 26 to 28 in Minneapolis.

At the opening board meeting held Monday, May 26 at the Radisson Hotel, the following present officers of Minnesota Blue Shield were re-elected: O. I. Sohlberg, M.D., Saint Paul, president; Richard R. Cranmer, M.D., Minneapolis, vice president; C. A. McKinlay, M.D., Minneapolis, secretary; and E. C. Bayley, M.D., Lake City, treasurer. Doctors Sohlberg, Cranmer, and Bayley also were re-elected to the Minnesota Blue Shield Board of Directors for three-year terms. Mr. F. Manley Brist, Saint Paul attorney, is legal counsel for the Minnesota Blue Shield Plan.

"Through April 30, this year, 34,738 Minnesota sub-

scribers received Blue Shield benefits amounting to $1,237,926 representing 43,285 medical-surgical services," Mr. Calvin stated.

"An interesting commentary," Calvin said, "is that 66.8 per cent (23,202) of the total Blue Shield medical-surgical claims through April 30, were incurred by dependents of family contracts. Payments on behalf of dependents alone totalled over $800,000 during the first four months of 1952."

"Since 1947 (inception of Minnesota Blue Shield) $7,899,825.12 has been paid for medical-surgical claims incurred by 216,516 subscribers who received Blue Shield benefits during this five-year period," Calvin reported.

"During 1951 Blue Shield gained 112,524 participants so that on December 31, 1951, 524,257 people were covered. Through the first four months of 1952 we have continued to grow with enrollment reaching 537,820 as of April 30. The Minnesota Medical Service Inc. is now tenth largest in the United States. This I think speaks well for the co-operation of the medical profession and the need for such a program."

"In 1951, $3,095,213 was paid to the medical profession—about a million dollars more than the previous year," Mr. Calvin concluded.

*Changes in Personnel and Board Directors.* Medical and other friends of J. Clifford Johnson will be interested in learning that he has accepted one of the top positions in the Public Relationship Department of the Pennsylvania Blue Cross plan with headquarters in Pittsburgh. Mr. Johnson came to Minnesota Medical Service Inc. from the Massachusetts Blue Shield plan in August, 1947, and has served as Manager of the Claims Department continuously since that time. His tenure of office has included the initial organization of the plan's operation and all the intermediate stages right up to the present high point in its development. The hosts of professional, business, office and other friends he has won throughout his service in Minnesota attest his qualifications to discharge the responsibilities of his new position.

Among other changes of prominent personalities have been the selections of Dr. C. M. Bagley of Duluth, and Dr. C. W. Moberg of Detroit Lakes as members of the Board of Directors, and Dr. N. H. Baker of Fergus Falls as a member of the Corporation. With deepest regret and reluctance, the Board of Directors accepted the resignations of Dr. W. A. Coventry of Duluth, and Dr. J. F. Norman of Crookston as members of the Board, and then appointed Dr. Bagley and Dr. Moberg, respectively, to fill their unexpired terms. Dr. Baker was selected to fill the vacancy in the corporate membership created by the death of Dr. W. L. Burnap of Fergus Falls. Included also in this same group of important changes was the appointment of Dr. E. C. Bayley of Lake City to fill the unexpired term of treasurer created by Dr. Coventry's resignation.

Doctors Coventry, Norman and Burnap have been closely identified with the Blue Shield plan since the earliest days of its inception. The entire medical profession is deeply indebted to each of these founders of Minnesota's prepaid medical care program. Even the

professional stature of the physicians chosen to replace them is a testimony of the invaluable contributions they have made.

On April 30, 1952, the Board of Directors authorized the appointment of Mr. Ben Stephens, Jr. to develop a physicians' and public relationship program. Mr. Stephens comes to Minnesota Blue Shield with a strong background and wealth of experience in this field. He served as a Judge Advocate General Officer in the Army during the last war, spent two to three years in personnel, claims and administrative work in the Veterans Administration and devoted eighteen months to public relations, educational and executive duties in the Graphic Arts Industry. Mr. Stephens has already put in operation the initial practices and procedures of a program which is designed to secure and maintain a better understanding of the doctors and Blue Shield of their mutual problems. However, pending replacement of Mr. Johnson, Mr. Stephens temporarily will assume the duties of Acting Manager of the Claims Department.

Recent changes to perfect the inner workings of Blue Shield and its processing of claims has been the addition of two highly qualified and experienced registered nurses as claims auditors. Headed by a particularly capable registered nurse who has been with Blue Shield in the capacity of Chief Claims Auditor for over two years, and with three highly trained, experienced and efficient claims examiners, the most technical feature of the Blue Shield claims processing has been brought to a highly satisfactory level by the acquisition of these two additional nurses.

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Hidden fees imposed by federal, state and local governments on a piece of merchandise as it passes through the economy—from its raw state until it reaches the ultimate consumer—constitute a large share of the cost. The taxes on a 10-cent candy bar amount to 3½ cents. Even the kids pay heavy taxes now.

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## INTERRELATIONSHIPS BETWEEN CARDIAC AND PULMONARY DISEASES

*(Continued from Page 671)*

vital capacity is usually markedly reduced. Of great importance is the slow expulsion of the air during the performance of procedure, expiration often requiring 5 to 10 seconds. The measurement of the vital capacity together with careful clinical and roentgenographic evaluation of the patient should enable us to distinguish primary cardiac disease with secondary pulmonary changes from primary pulmonary disease with secondary effects upon the heart.

# BOOK REVIEWS

**Books listed here become the property of the Ramsey, Hennepin and St. Louis County Medical Libraries when reviewed. Members, however, are urged to write reviews of any or every recent book which may be of interest to physicians.**

### Books Received for Review

A TEXTBOOK OF PATHOLOGY. Seventh Edition. E. T. Bell, M.D., Emeritus Professor of Pathology, University of Minnesota, Minneapolis. 1008 pages. Illus. Price $12.00, cloth. Philadelphia: Lea & Febiger, 1952.

SURGERY OF THE CHEST. A Handbook of Operative Surgery. Julian Johnson, M.D., D.Sc. (Med.). Professor of Surgery, School of Medicine and Graduate School of Medicine, University of Pennsylvania; and Charles K. Kirby, M.D., Assistant Professor of Surgery, School of Medicine, University of Pennsylvania. 387 pages. Illus. Price $9.00, cloth. Chicago: Year Book Publishers, 1952.

THE HUMAN PELVIS. Carl C. Francis, A.B., M.D. Assistant Professor of Anatomy, Department of Anatomy, Western Reserve University, Cleveland, Ohio. 210 pages. Illus. Price $5.00, cloth. St. Louis: C. V. Mosby Co., 1952.

THE STORY OF THE ADAPTATION SYNDROME. Hans Selye, M.D., Ph.D. (Prague), D.Sc. (McGill), F.R.S. (Canada). Professor and Director of the Institut de Médecine et de Chirurgie expérimentales Université de Montréal. 225 pages. Illus. Flexible cover. Montreal: Acta, Inc., 1952.

INTERNAL MEDICINE: ITS THEORY AND PRACTICE, originally ed. by John H. Musser, B.S., M.D., F.A.C.P., Late Professor of Medicine in the Tulane University of Louisiana, School of Medicine, New Orleans, La. 5th ed. ed. by Michael G. Wohl, M.D., F.A.C.P., Associate Professor of Medicine, Temple University School of Medicine; Chief of Nutrition Clinic, Philadelphia General Hospital; Chief of Endocrine Clinic, Temple University Hospital. With 80 Contributors. 1563 pages. Illus. Cost $15.00. Philadelphia: Lea & Febiger, 1951.

This new edition of Dr. John Musser's original book was well received and gave much enjoyable reading to the reviewer. The new popular two-column format is restful even after several hours of reading.

The various authors have divided their discussions of the individual diseases in a similar manner throughout the book. This makes it a more rapid job to use this book as a reference for reviewing one particular aspect of a disease.

The relative dearth of illustrations in this book is compensated for by the quality of those included and the good descriptions in the text itself. Suggested therapy is included for most diseases and is up to date. The use and misuse of ACTH and cortisone is well described for the appropriate diseases.

A new chapter on "Genetics and Medical Practice" has proved useful for a consultation during the period of reviewing this book. It gives ready help to those questions parents and friends of abnormal offspring often bring to the physician. The other new chapters are much needed and include: the general adaptation syndrome, antibiotics and chemotherapy, rehabilitation of the chronically ill, geriatrics and the psychosomatic aspects of medical practice.

This new edition should continue to be a favorite in the libraries of all practitioners—both general and specialists.

DONALD W. KOZA, M.D.

## IN MEMORIAM
### WILLIAM A. KENNEDY

*(Continued from Page 688)*

special senses at the University of Edinburgh and the Mayo Clinic.

He was a former chief-of-staff of St. Joseph's Hospital in Saint Paul and a former member of the advisory board of the hospital. He was a member of the Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association. He was also a member of the Saint Paul Clinical Club, the University Club of Saint Paul and the Serra Club. During World War I he went overseas as a medical officer with Base Hospital 26.

Dr. Kennedy is survived by his wife, Helen, and two daughters, Mary Francis and Mrs. J. Thomas Simonet. A brother, John, livês in Minneapolis, and a sister, Mrs. Fred Huntington, in Los Angeles.

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## MEDICAL ECONOMICS

*(Continued from Page 681)*

advances in the field of human relations comparable to the colossal strides made in technology. "Actually there is no reason why this should be so," Dr. Klotsche went on, "for our fundamental beliefs and ideals provide us with a basis for making it possible for human beings to live together harmoniously." That basis is the "belief that every individual possesses dignity and worth and has the right to be considered a person at all times regardless of race, color, creed, economic status or political belief."

### Multiplicity an Asset

Dr. Klotsche told doctors and their guests that America is one nation which has taken advantage of its contrasts and has actually cultivated its own multiplicity to the point where it is an asset. He concluded, "America is a land made up of many nationalities, races, traditions and faiths. It was born in diversity and has prospered and grown because we have cultivated multiplicity. . . . The United States is large. It does contain multitudes. But it is this incorrigible pluralism that has given us such great vitality. This diversity confounds the stranger in our midst, bewildered by the existence of persons of so many different races, nationalities, and creeds. But to us this diversity is no problem at all. It is in fact our greatest asset."